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THE URINE AND FECES IN DIAGNOSIS

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PREFACE

LARGE and exhaustive treatises on clinical and laboratory methods of diagnosis are numerous, but a compact, handy and trustworthy guide to the combined study of the urine and the feces is still a desideratum. It has been the aim of the authors to supply this, bearing in mind throughout the actual daily needs of the working practitioner.

The importance of urinary examination for purposes of diagnosis of diseases of the kidneys, as well as for general perversion of bodily functions, needs no special comment. Every practitioner of medicine or surgery makes use of urinalysis. It has been the object of Dr. Hensel in preparing the chapters on the urine, so to present this many-sided subject that the required diagnostic indications may be obtained with the minimum of effort compatible with accuracy. However, the more technical procedures have not been omitted, nor have the needs of the advanced student of urinology been neglected.

The presentation of the accumulated knowledge concerning the feces in the chapters upon that subject, which are largely from the pen of Dr. Weil, must prove of great clinical value to every practitioner of medicine. The systematic study of the feces has been much neglected by physicians, pediatrists alone evincing a commensurate interest in this branch of diagnostic medicine. Probably this has been due in large part to a scanty and scattered literature; but, thanks to the unremitting labor of German investigators, notably Schmidt and Strasburger, some order has been brought out of the chaos of coprologic research, and in the present volume, for the first time, many important facts are rendered accessible to English-speaking students.

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We are particularly indebted, in the chapters on Bacteriology, to the masterly work of Ford, done largely under the auspices of the Rockefeller Research Fund. His investigations have laid the foundation of a thorough knowledge of the intestinal bacterial flora, and the results of his work have been closely followed in this manual.

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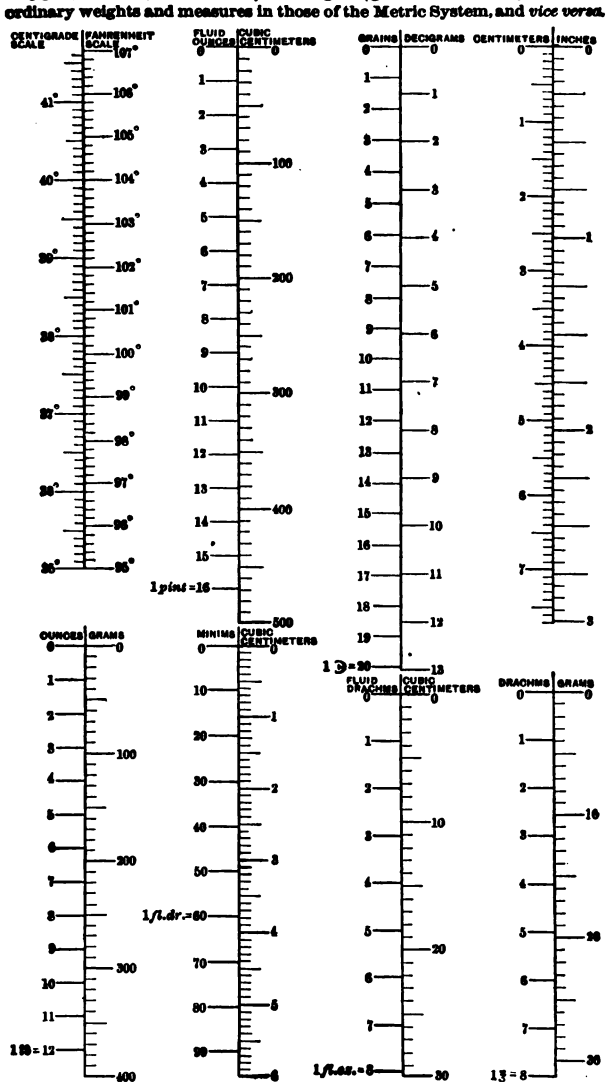
COMPARATIVE SCALES, showing at a glance the exact equivalent of ordinary weights and measures in those of the Metric System, and *vice versa*.



URINALYSIS.

CHAPTER I.

GENERAL PATHOLOGY AND PHYSIOLOGY OF THE KIDNEYS. THE MECHANISM OF URINARY SECRETION.

The parts of the kidney immediately associated with the secretion of urine are the glomerular capsule, the convoluted tubes and the loop of Henle, while the straight collecting tubules probably have no secretory functions. The most complex portion of this tract is the glomerulus. It consists of an afferent vessel, which breaks up into a number of capillaries to form an intricate meshwork, the separate vessels of which again unite to form an efferent vessel. The capsule is an expansion of the uriniferous tubule, and consists of two layers, the inner one of which closely invests the tuft of capillaries, and is made up of a single layer of flattened endothelial cells.

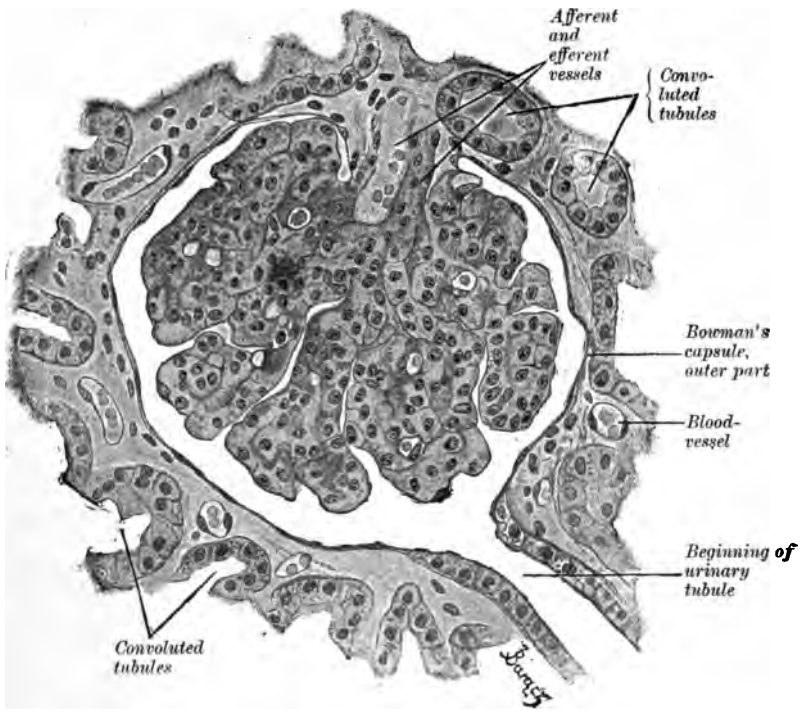
It is evident that most favorable conditions exist here for filtration. The blood-stream is considerably slowed, owing to the width of the stream-bed, and the blood itself is separated from the capsular space by only two layers, the capsular and the glomerular endothelium.

In accordance with the fact that the secretory apparatus of the convoluted tubules and the loops of Henle remove different substances from the blood than the glomeruli, the cells interposed between blood and urine here present a different structure. They are generally cuboidal or cylindrical and granular in appearance, and show a peculiar striation toward their base. In the collecting tubules the lining cells are clearer; they increase in thickness as they approach the apex of the papilla, and are probably less highly differentiated cells.

With the advance of physiological methods of research, theories relating to the mechanism of urinary secretion have undergone several modifications. While formerly simple mechanical filtra-

tion was called upon to explain the formation of urine, it is now generally assumed that the cells lining glomeruli and tubule possess active secreting properties. Ludwig formerly believed that water, inorganic salts and organic principles were simply filtered out of the blood by the glomeruli, the complete, but diluted, urine then becoming concentrated in the subsequent passage of this liquid along the convoluted tubules. Later physiological and histological study, however, seems to point to the fact that the

FIG. 1.



From a section through the cortex of an ape's kidney. A Malpighian corpuscle, together with the beginning of the urinary canal, is shown. X 350. (Szymonowicz.)

larger amount of nitrogenous matter is actively eliminated by the cells of the convoluted tubules. Briefly, this theory is based upon the following observations: In birds uric acid takes the place of the urea of mammals. If the ureters are ligated, uric acid crystallizes out in the tubes, but never in the Malpighian corpuscles. Similarly, indigo-carmine, when injected into the circulation of a living animal, will be precipitated in the tubular cells.

Certain histological changes in these cells have, furthermore, been described by various authors which point to metabolic activity

FIG. 2.

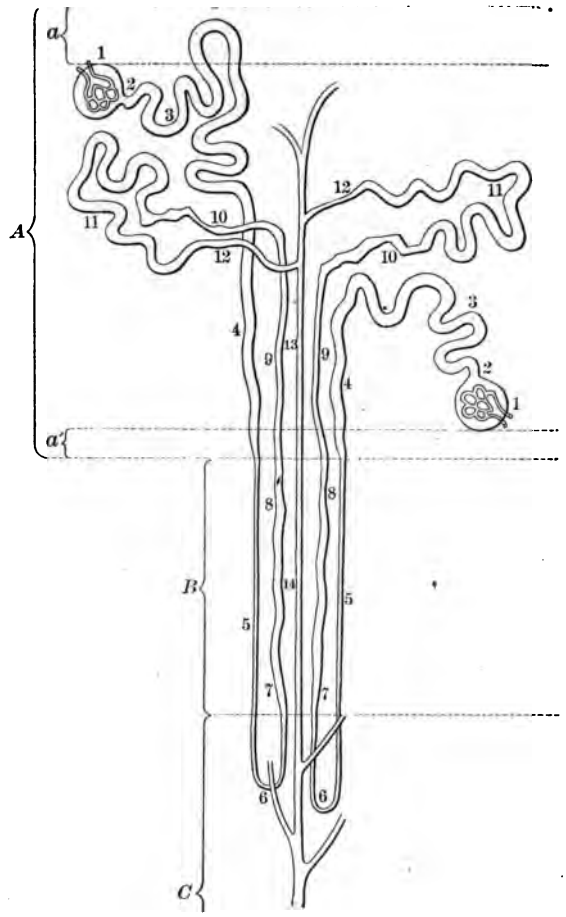


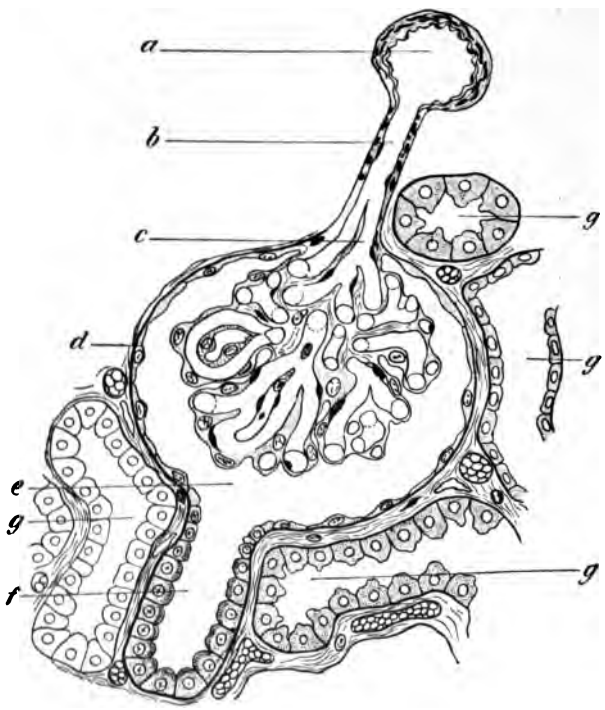
Diagram showing the course of the renal tubules within the kidney. (Klein.) *A*, cortex; *a*, subcapsular portion destitute of Malpighian bodies; *a'*, inner portion, also devoid of Malpighian bodies. *B*, boundary. *C*, portion of the medulla at the base of the pyramid. 1, Bowman's capsule surrounding the glomerulus; 2, neck of the capsule and beginning of the uriniferous tubule; 3, first convoluted tubule; 4, spiral portion of the first convoluted tubule in the medullary ray; 5, descending limb of Henle's tube; 6, Henle's loop; 7, 8, 9, ascending limb of Henle's tube; 10, irregular transition to the second convoluted tubule; 11, second convoluted tubule; 12, transition from second convoluted tubule to the collecting tubule; 13, 14, collecting tubule, joined below by others to form the excretory duct, which opens at the apex of the pyramid.

more pronounced than would accompany the simpler processes of filtration and diffusion. Secretory function on the part of the

glomerular endothelium is also highly probable, since many pathological products, such as albumin, hemoglobin and sugar, are excreted here.

The kidneys are richly supplied with nerves, chiefly of the sympathetic plexus. But their relation to the process of secretion is not well understood, since all stimulation produces alterations in

FIG. 3.



Sketch of a Malpighian body from kidney of a rabbit; *a*, interlobular artery; *b*, afferent vessel; *c*, capillary springing from afferent vessel; *d*, Bowman's capsule, with epithelial lining reflected upon the surface of the glomerulus; *e*, cavity of the capsule into which the watery constituents of the urine are first discharged; *f*, beginning of a uriniferous tubule; *g*, convoluted tubules of the labyrinth. Between these tubules and the capsule are capillary bloodvessels derived from the efferent vessel (which is not shown, but emerges from the capsule near the afferent vessel, on a different level from that represented). These and other structures are held in place by an areolar tissue, containing lymphatic spaces, some of which are represented. (Dunham.)

vascular tension, which alone would explain changes in secretion. Direct connection between nerve-fibres and epithelial cells has not yet been demonstrated, and it is probable that the nervous system affects renal function solely through the vessels.

It is evident that an examination of the urine will give a fairly

clear idea of the condition of the kidneys, but it is not only in renal disease that urinalysis is of extreme, indispensable value. While

FIG. 4.

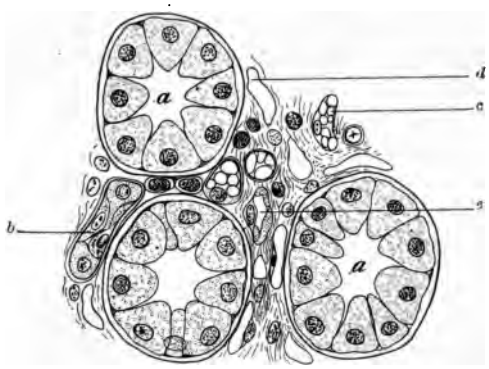
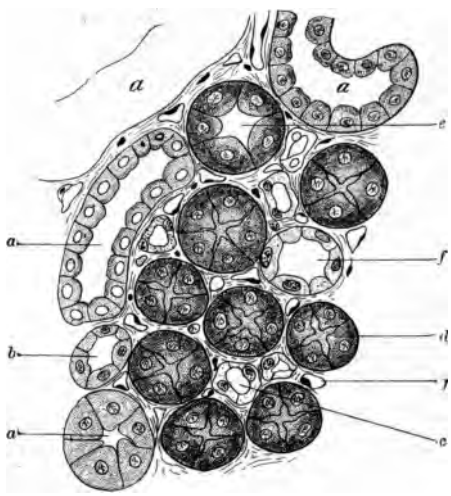


FIG. 5.



Sections from a rabbit's kidney, made perpendicular to the course of the straight tubules.

Fig. 4. Through a portion of the pyramid: *a*, lower portions of the collecting tubules (excretory ducts); *b*, Henle's loop in tangential section; *c*, capillary bloodvessels; *d*, lymphatic; *e*, descending limb of Henle's tube. (Dunham.)

Fig. 5. Through part of a medullary ray and the adjoining labyrinth; *a*, *a*, *a*, *a*, convoluted tubules in the labyrinth; *b*, spiral tubule; *c*, descending limb of Henle's tube; *d*, ascending limb of Henle's tube; *e*, irregular tubule; *f*, collecting tubule; *g*, capillary bloodvessel. (Dunham.)

the presence of albumin will in many cases point to a grave kidney lesion, the intimate relation of the organs with the cardio-vascular

system makes a close analysis in circulatory disturbances equally as imperative. Owing to the fact that the kidneys filter out foreign elements, or an excess or diminution of normal elements from a fluid which has come into intimate contact with all the organs of the body, the presence or absence of constitutional disease, or of disease in some distant organ, may often be disclosed. It cannot be impressed too strongly upon the practitioner that no patient should leave his office without a thorough, if not complete, urine examination. How often does a headache form one of the symptoms of nephritis; an excess of uric acid point to a gouty disturbance, and a cataract to diabetes. The probabilities of typhoid may be considerably increased in doubtful febrile conditions, and an excess of indican may materially assist in the diagnosis of an intestinal obstruction. The surgeon may successfully diagnose a doubtful hematuria as tuberculosis or tumor where all physical signs fail, and by means of ureteral catheterization he may even decide on which side the lesion is.

FIG. 6.

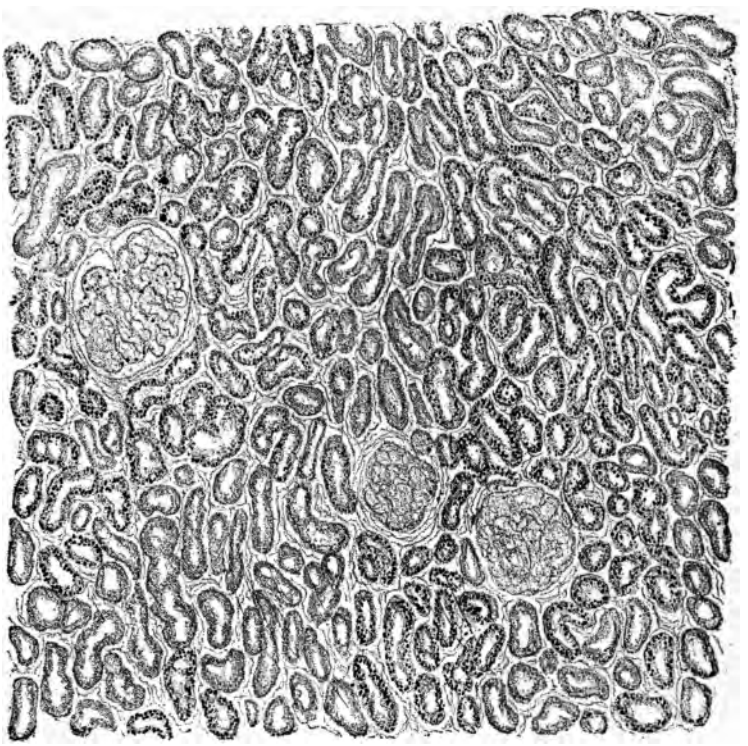
Cloudy swelling of renal epithelia. (After Futterer.)

On the other hand, too much should not be expected from laboratory technique. Many of the foreign elements found are common to several disorders, and while diagnosis may be materially assisted, it will not always be absolutely cleared up. In this age of accurate laboratory work there is a growing tendency to lay considerable stress upon the disturbed excretion of inorganic salts in constitutional disorders, but it is doubtful if this subject is as yet ripe for practical application. In another respect urinalysis has proved disappointing. While renal disease may generally be detected with ease, it is still impossible to say in any given case if sufficient renal tissue is present to permit the vital processes to go on. Cryoscopy, it is true, has proven of enormous value to the surgeon, and, by contraindicating operation, has saved many a

patient from a quick death by uremia. But later researches have shown that this method, though simple and practical, is far from accurate (see Chapter XI).

It may not be amiss to touch briefly upon the lesions which commonly affect the kidneys, and their relation to the composition of the urine. Every degenerative or inflammatory process affects most seriously the most highly differentiated element of the kidney

FIG. 7.



Fatty degeneration of the kidney. The fat stained black with osmic acid. X 50. (Schmaus.)

—the renal secreting cell. The protoplasm of the cell and its nucleus will break down and pass into the urine. By far the greater portion of the albumin, however, is serum albumin and serum globulin, derived directly from the blood, since the pores of the filtering apparatus have become coarser and the secreting function is seriously interfered with. Since the glomerular endothelium is the most delicate of all the elements, the tubular cells will be affected later, and only in the more severe disturbances. It

is still doubtful whether tubular degeneration alone will permit an excretion of albumin, for in cantharides poisoning, where the changes are most marked in the lining cells of the convoluted tubules, albuminuria is often absent.

Other phenomena of nephritis which are responsible for the characteristic changes of the urine are the circulatory disturbances which occur in the acute forms, as congestion; in the chronic types, as cardiac hypertrophy, arteriosclerosis and variations in vascular tension. A slowing of the blood-stream will bring less nutrition to the cells, disturb their metabolism, and thus make them more permeable for albumin.

FIG. 8.

Parenchymatous hemorrhagic nephritis with desquamation in the glomeruli. In the capsule of Bowman lie many desquamated epithelia. In many tubules there are masses o red cells. Above to the left a focus of round-cell infiltration in the stroma. Fibrous increase about the glomerulus. X 250. (Schmaus.)

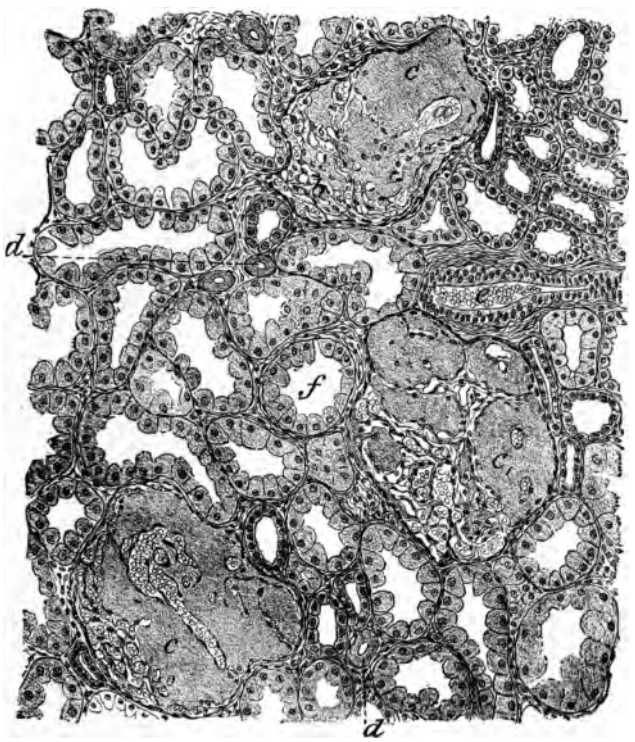
Vascular disturbances will also bring about changes in color, amount and concentration, which are more or less characteristic for the different forms of nephritis. The amount of water excreted will rise if the amount of blood which circulates through the kidneys is increased; that is, if the arterial pressure rises without change in the lumen of the vessels, and without increased resistance, or when the pressure remains normal, but the vessels dilate. The former condition is often seen in chronic interstitial nephritis, for arterial tension and cardiac hypertrophy almost invariably accompany this condition. If digitalis be given to patients with

cardiac disease, arterial pressure will rise and increased diuresis will follow.

The second condition, normal pressure, with dilated vessels as a cause for an increased secretion of urine, is seen after dividing the renal nerves, and may be the cause of polyuria in insipid diabetes.

Less blood carried to the kidneys will mean less secretion of

FIG. 9.



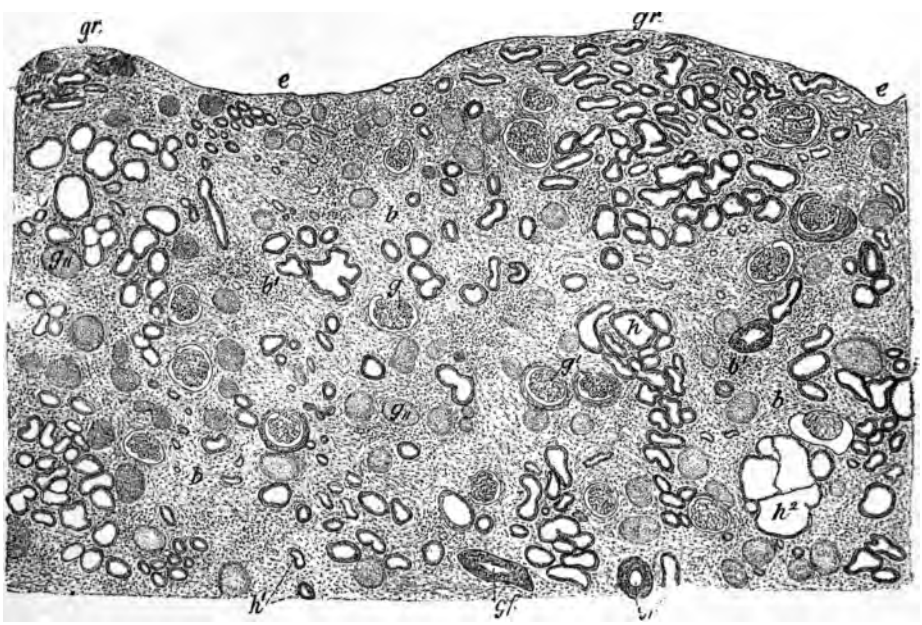
Amyloid degeneration in the kidney. *a*, *b*, glomerular vessels, still permeable; *c*, *c*, c_1, amyloid vessels; at c_1 the lumen can still be traced; *d*, amyloid capillaries of the stroma *f*, tubule; *e*, artery. × 40. (Schmaus.)

urine. This is common when the renal vessels are also involved in the general increase of arterial tension, or when they retain their normal width, but the arterial pressure is lowered or the venous pressure increased, so that the blood-flow within the kidney is retarded. The general increase in tension is best seen in asphyxia, strychnine poisoning, epileptic and eclamptic convulsions, the retardation of blood-flow in thrombosis or cardiac weakness. Retardation is also one of the phenomena of inflammation, and it is

but logical that an inflamed kidney should excrete subnormal amounts of urine.

Another cause for diminished excretion is probably to be found in the occlusion of the tubules by detritus from the renal cells, casts, etc. We cannot say, however, if this deposit is caused by the diminished pressure or whether it really forms an impediment to the free flow of urine Obstructions lower down, such as stenosis of the ureter, will naturally diminish the speed of excretion.

FIG. 10.



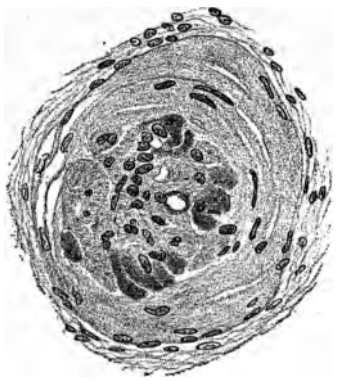
Chronic interstitial nephritis. b, b^1, areas of atrophy and induration; h^1, atrophic tubule; g, glomeruli still persisting; g^1, destroyed; b^1, round-cell infiltration; e, depression of the surface; gr, granules where the tubules are less affected; h, wider tubule; h^2, cystic tubule; gf, thickened vessels. X 30. (Schmaus.)

It is an interesting fact that but one kidney is necessary for life, provided sufficient time elapses to permit the organ to increase in size and approximately perform the functions of two. While acute and chronic nephritis, as a rule, are bilateral, surgical affections, such as abscess and tuberculosis, frequently affect only one organ. In the more chronic processes sufficient opportunity is given to the remaining healthy organ to hypertrophy, so that life need not be seriously menaced by a nephrectomy.

The intimate relation of proper renal function to the well-being

of the entire body is clearly seen in the later stages of chronic nephritis. The constant loss of albumin is hardly sufficiently large

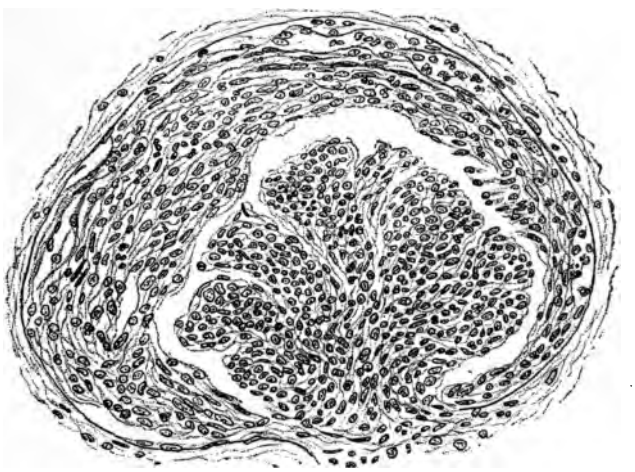
FIG. 11.



Glomerulus in degeneration. Thick hyaline capsule tightly applied to the tuft, its cavity lost, some vascular coils hyaline (darker); externally loose connective tissue. X 350. (Schmaus.)

to lead to a cachexia, but where much renal tissue has been destroyed by a parenchymatous or interstitial process, a retention of

FIG. 12.



Growth of connective tissue into the capsule of Bowman from the hilum, the original limits as a darker line. X 350. (Schmaus.)

excrementitious products occurs, which gradually or suddenly will lead to the intoxication known as uremia. Strangely enough, our

knowledge concerning the principles which are directly responsible for this condition are singularly incomplete, and this is hardly the place to enumerate the various theories which have been advanced at one time or other. We seem to be just as far to-day from a plausible explanation of the peculiar nervous and cardiovascular symptoms which mark uremic intoxication as we were fifty years ago.

In examining a urine, it must not be forgotten that the excretion passes through the ureters and is stored in the bladder some time before it is voided, and that in both places it may undergo considerable change. To determine whether a variation from the normal will point to a renal or vesical lesion may at times be a difficult task for the physician, but, fortunately, ureteral catheterization will now enable him to examine the urine from each kidney directly.

CHAPTER II.

PHYSICAL PROPERTIES OF URINE.

Amount.—Normally the amount of urine varies within very wide limits, the figures generally given being 1,000-2,000 c.c. for twenty-four hours. Age and sex have but a moderate influence, but the effect of ingested fluid, external temperature and exercise is very marked.

During hot weather the excretion of water by the skin is more active, and the figures frequently are low, even though more water is taken. Generally speaking, the secretion of urine varies considerably during different parts of the day, it being greatest several hours after a meal and least during the first hours of the night.

In morbid conditions the urine may be entirely suppressed, or it may be diminished or increased. Suppression of urine must be carefully distinguished from retention of urine, in which there is some obstruction to the flow in the genito-urinary tract, beyond the secreting apparatus. Diminished flow is generally known as oliguria, increased flow as polyuria.

Complete suppression (anuria), if not a hysterical symptom, is generally an accompaniment of uremia, and frequently precedes death. In cases without distinct renal history, retention should be ruled out by catheterization. Rarely the obstruction may be higher than the bladder, as in stone obstructing the ureters, or in accidental ligation of both ureters. It is even possible for a normal kidney to cease secreting, owing to reflex nervous influences, if the opposite ureter is obstructed (reflex anuria), though this occurrence has been doubted and is not as frequent as was formerly believed.

A diminished amount of urine is a common symptom in congestion of the kidneys, such as accompanies cardiac disease, with loss of compensation and many febrile disorders, since heart action and blood-pressure are generally lowered and less blood flows through the renal vessels.

Oliguria is also a prominent symptom of acute nephritis and chronic parenchymatous nephritis, owing to the degeneration of the renal cells and the mechanical resistance offered by the exudate. Less common causes for diminished urinary flow are pressure upon

the vena cava, owing to tumor or excessive ascites, thrombosis of the inferior vena cava or the renal vein, hepatic disease accompanied by obstruction to the flow of blood in the liver, cholera, severe hemorrhage and various nervous conditions.

Polyuria is common to two diseases—diabetes mellitus and chronic interstitial nephritis—but in either case a clear explanation of this symptom does not exist. Many organic and functional nervous diseases (hysteria, diabetes insipidus, epilepsy, tabes, etc.) are characterized by an excessive flow of urine, and active diuresis is often seen during the absorption of exudates in convalescence from prolonged fevers (epicritic polyuria) and with multiple myelomata of the bones. The most excessive degrees of polyuria have been observed in diabetes mellitus and insipidus (up to 43,000 c.c.).

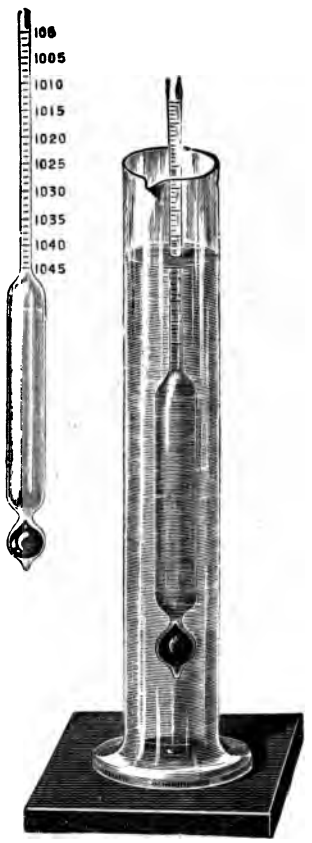
Appearance.—Normal urine, when freshly voided, forms a clear, transparent, amber-colored fluid. In summer, alkaline salts, or organic salts which readily become alkaline in the body, are frequently ingested in large amounts with fruit, etc., so that the urine, though fresh, may be turbid, owing to the precipitation of phosphates. Similarly, in winter uric acid and urates may precipitate out in the form of a brick-dust sediment or a diffuse milky turbidity if the urine is kept in a cold place. The phosphates are redissolved by slightly acidifying with acetic acid, the urates by gently warming. In most urines a distinct cloud (nubecula) will slowly settle to the bottom if allowed to stand for several hours. This cloud consists of mucus in which are entangled desquamated epithelial cells. In warm weather a diffuse turbidity will form, owing to the proliferation of bacteria. This should be avoided, since such urines are difficult to filter and the more delicate morphological elements are often destroyed. Pathological turbidity may be due to pus cells or bacteria from the kidney itself, its pelves, bladder or urethra. In women a certain amount of turbidity is often due to admixture with menstrual blood or vaginal discharge.

Normal urine varies in color from a pale yellow to a dark amber, depending upon its degree of dilution. Very pale urines generally go with polyuria, and are therefore common in chronic interstitial nephritis, diabetes and hysteria. Dark urines indicate concentration, and are met with in acute and chronic parenchymatous nephritis, in the congestion of heart disease and in fevers. Oftentimes the urine lacks its characteristic yellow or amber hue, and is differently colored.

If orange, urobilin may be present; if greenish-yellow or

greenish-brown, with yellow foam, bile; if red or reddish-black, blood; if green, phenol, creosote or guajacol; if blue, methylene blue; if pink, pyramidon; if red, hematoporphyrin, santonin, the principles of rhubarb, etc.; and if milky, fat in emulsion. In the presence of alkapton, melanin or phenol the urine may be dark when voided or change color soon after.

FIG. 13.



Urinometer. (W. Simon.)

Odor.—Owing to the presence of volatile acids, urine has a distinct, characteristic odor. Alkaline, decomposed urine is ammoniacal, while the ingestion of oil of turpentine, asparagus, etc., also modifies the smell.

Specific Gravity.—The determination of the specific gravity of urine gives an idea of the total amount of solid substances. Since the most abundant of these are urea and sodium chloride, the

concentration of any given urine depends in greater part upon these. The normal figures vary between 1,005 and 1,030, usually 1,015-1,025.

Since variations occur from hour to hour, it is more accurate to employ the mixture obtained during twenty-four hours. A sample of this is poured into a cylindrical glass, care being taken to avoid foaming. The usual urinometer is an ordinary hydrometer accurately graduated between 1,000-1,050. It is simply dipped into the fluid in the cylinder, and the reading taken at the level where it floats. While this method is simple and accurate, considerable difficulty may be experienced where the quantity of urine at hand is so small that it does not fill the cylinder. Sufficiently accurate results can then be obtained by diluting once with water and multiplying the last two figures of the result by 2. With still smaller quantities the following methods are at our disposal: 1. Jolle's hydrometer, requiring 20-25 c.c. to float. 2. Mohr-Westphal balance, requiring about 15 c.c. This instrument is most accurate, but too expensive for ordinary work. 3. Pyknometers. These require a good deal of skill and a very expensive balance. 4. The use of a mixture of two fluids of different specific gravity, such as are employed for blood-work. 5. The Urinopyknometer of Saxe. This instrument is very easy to handle, requires only a small amount of urine and is very cheap in price. It is shaped like an ordinary hydrometer, but is provided with a cup above the stem, into which 5 c.c. of urine are placed. By then floating in distilled water, at 15 c.c., an accurate reading is possible.

An approximate idea of the total solids contained in urine may be obtained by multiplying the last two figures of the specific gravity by 2. Thus, if the specific gravity of the voided urine is 1,015, there will be about 30 grams of solid matter to the litre. According to Haeser, more accurate results will be obtained by multiplying by 2.33.

A low specific gravity is obtained after the use of much water or the administration of diuretics in chronic interstitial nephritis, diabetes insipidus and other nervous forms of polyuria. As a rule, low specific gravity accompanies an abundant excretion and a high specific gravity a scant amount of urine, but a diminished amount with high specific gravity is common in many chronic diseases, and toward the fatal termination of acute disease, in some cases of edema and after copious vomiting, diarrhea and sweating. In diabetes mellitus there is generally polyuria with high figures, owing to the presence of varying amounts of glucose.

Reaction.—Urine when voided is most usually acid, but may also be amphoteric or alkaline, without indicating lesion. Blue and red litmus paper are generally employed to indicate the reaction. The acidity is caused not by uric acid, but by disodium acid phosphate, NaH_2SO_4; alkalinity by an excess of carbonates and of neutral sodium phosphate and an amphoteric reaction by the presence of certain proportions of both acid and neutral phosphate. Highly concentrated urine is often very acid, while the ingestion of food rich in organic salts, which are burned up into alkaline carbonates, will increase the alkalinity of the blood and more than neutralize the acid salts in the urine. The free excretion of gastric juice after a large meal will also tend to change the reaction. Even in disease the urine is acid in the majority of cases, unless there is inflammation, or stagnation in the bladder. The same changes that occur when urine is allowed to stand exposed to the air are then apt to follow: the urea is simply converted into ammonium carbonate, owing to micro-organismal activity.

In order to determine the degree of acidity, Freund has recently devised the following method, which is rather complicated for ordinary use:

The total amount of phosphoric acid is determined in 50 c.c. of urine, according to the usual method. Ten c.c. of a 12.2 per cent. solution of barium chloride for every 100 milligrams of phosphoric acid present are then added to another 50 c.c. to precipitate the monacid phosphates. After the addition of the barium the mixture is diluted up to 100 c.c., filtered and the phosphoric acid estimated in 50 c.c. of the filtrate. Supposing that the total amount of phosphoric acid amounted to A and the last phosphoric acid determination to B, the relative proportion of A to B would be determined according to the equation

$$A : B :: 100 : X \qquad X = \frac{100\,B}{A}$$

The total acidity for twenty-four hours is then calculated by multiplying X by the number of 100 c.c. voided and the total acidity per hour by dividing this number by 24.

If the urine is alkaline and cloudy, the sediment is dissolved by shaking with one-tenth normal hydrochloric acid and deducting the amount from the total acidity.

The above method of determining the total acidity is not frequently employed. Titration with decinormal sodium hydrate

solution, using phenol-phthalein as indicator, is inaccurate, but will often suffice for comparative figures. The depth of the red obtained on using blue litmus will do, however, for clinical work.

Molecular Concentration and Osmotic Pressure.—Cryoscopy, or the determination of the freezng-point of the urine, is a new department of urinalysis which is coming more and more into favor, and which gives valuable information concerning the functional activity of the kidneys, though not as infallible as first believed. It is based upon the observations of Raoult (a) that all

FIG. 14.

Beckmann's apparatus. (Simon.)

solid, liquid or gaseous substances, when dissolved in a liquid, will lower the freezing point of that liquid; (b) that the degree to which the freezing point is lowered depends upon the amount of substance which is in solution, and (c) that equimolecular solutions have like freezing points. Distilled water freezes at 0° C., urine in health at 0.9° C. to 2° C. This figure is generally designated by the capital Greek letter Δ, while the corresponding small letter δ signifies the freezing point of blood-serum, which is normally 0.56° to 0.58° C. Since more constant, the latter is generally preferred, though very valuable information may be

obtained by ureteral catheterization and separate determination of both urines.

A freezing-point above — 0.9° C. indicates low molecular concentration, and shows better than the amount of urea or the specific gravity that the function of that particular kidney is seriously interfered with, perhaps to such an extent that operation is contraindicated. A comparative high congealing point of the urine goes hand in hand with a depression of the freezing-point of the serum, since this will possess higher molecular concentration, owing to the presence of retained excrementitious products.

Cryoscopy is practiced by means of a very simple apparatus, whose component parts are a delicate thermometer graduated in hundredths of a degree, a test tube for the urine or serum, which is provided with a stopper perforated for the thermometer, and a platinum stirring-rod, and finally a large glass jar, which is filled with ice and salt and also contains a stirring-rod. If the thermometer be watched as the test-tube is placed into the freezing mixture, the column of mercury will gradually fall, then suddenly rise and reach a stationary point, which corresponds to the congealing-point of the fluid examined. In every case distilled water should be employed first. The difference between the freezing-point of this and of the urine will then indicate the number of degrees below zero. It is necessary to keep the fluid in constant motion by agitating with the stirring-rod.

CHAPTER III.

CHEMISTRY OF URINE.

There are certain reactions which all urines have in common. Briefly, they are the following:

1. Acids on warming will darken the urine and cause a precipitation of uric acid crystals when cooled.
2. Caustic alkalies cause turbidity and precipitation of earthy phosphates.
3. Lead acetate throws down a white precipitate, consisting of chloride, phosphate and sulphate of lead, together with pigments, so that on filtering the urine may be almost colorless. A slightly colored urine is especially desirable where a large column of urine is examined by light, as in polariscopy.
4. Silver nitrate gives rise to a white precipitate of chloride and phosphate of silver.
5. Barium chloride throws down the phosphates and sulphates.
6. Ferric chloride in the presence of sodium acetate precipitates the phosphates.
7. Alcohol gives a turbidity, which disappears on diluting with water.
8. Boiling will have no effect unless the urine is amphoteric or alkaline, when the earthy phosphates will precipitate.

Urine is always a complex fluid, which contains many substances in solution. These may be divided into organic and inorganic.

ORGANIC INGREDIENTS.

Urea	30	grammes	in	twenty-four	hours
Uric Acid	0.7	"	"	"	"
Kreatinin	1.0	"	"	"	"
Hippuric Acid	0.7	"	"	"	"
Other bodies	2.6	"	"	"	"

Xanthin bodies, oxalic and oxaluric acids, volatile fatty acids, lactic and succinic acids, carbohydrates, glycerino-phosphoric acid, salts of phenyl- p-cresyl-, pyrocatechin-, indoxyl- and skatoxyl-sulphuric acids, phenol, p-oxyphenylic and p-hydrocumarinic acids, glycuronic acid, pigments, ferments and other substances of unknown composition.

INORGANIC INGREDIENTS.

Hydrochloric Acid	9.35	grammes	in	twenty-four	hours
Sulphuric Acid	2.5	"	"	"	"
Phosphoric Acid	2.5	"	"	"	"
Nitric Acid	0.1	"	"	"	"

COMBINED WITH

Sodium (Na_2O)	7.9	grammes	in	twenty-four	hours
Potassium (K_2O)	3.0	"	"	"	"
Ammonium (NH_3)	0.7	"	"	"	"
Calcium (CaO)	0.3	"	"	"	"
Magnesium (MgO)	0.5	"	"	"	"
Iron, trace					

GASES.

Oxygen	1.0 c.c.
Carbon Dioxide	24.0 "
Nitrogen	10.16 "

Urea. ($[NH_2]_2CO$).—In health, and generally in disease, the amount of urea in the urine is a good index of the total nitrogenous excretion, since it usually forms about 85 per cent. of all nitrogenous bodies. There is no doubt that urea represents the proteid tissue waste, but as yet there is considerable speculation upon the intermediate principles. According to the most popular theory, the waste nitrogen leaves the tissues as the ammonium salt of paralactic acid. This is then changed into ammonium carbonate by the liver, and finally into urea through the intermediary formation of ammonium carbamate.

Urea is derived in part from the organized albumin, in part from the reserve albumin circulating in the blood. A clear idea of the tissue waste going on within the body can generally be obtained by a quantitative estimation, yet in some diseases the proportion between urea and other nitrogenous principles is so disturbed that a total nitrogen determination will become necessary. This applies especially to acute yellow atrophy of the liver, where the urea may disappear from the urine, and to the leukemias and gout, where uric acid is often in excess.

Since every urine contains some urea, a qualitative analysis will hardly ever be necessary, unless one wishes to decide if a certain fluid is urine. The quantitative analysis is, however, of the greatest importance, since, like cryoscopy, it gives a good idea of the functional activity of the kidneys. The normal amounts vary between 10 and 20 grammes per litre, and bear a direct relation to the

specific gravity; thus concentrated urines contain much, dilute urines little of this substance. In disease the amount is increased when metabolism is more active, as in fevers. This is especially marked in fevers terminating by crisis. Excessive excretion may also occur in diabetes mellitus, in part due to the increased consumption of proteids, in conditions associated with dyspnœa, in pernicious anemia, leukemia, scurvy and certain nervous affections, and after the use of caffeine, chlorides, carbonates and some of the alkalies.

Diminished elimination of urea is most pronounced in serious hepatic disturbance, such as acute yellow atrophy, cirrhosis and carcinoma, because urea is no longer formed, and in renal disease because it can no longer be excreted. Since the convoluted tubules are chiefly concerned with the excretion of urea, a nephritis involving chiefly the glomeruli need not be accompanied by retention of nitrogenous matter. There is also a deficiency of urea in some nervous and mental disorders.

Uric Acid.—Though the main nitrogenous principle in the urine of birds and reptiles, uric acid plays but a subordinate rôle in mammals and man, as compared with urea. It is, in all probability, derived from the nuclear substance of cells, through bases spoken of collectively as xanthin, purin or alloxur bodies (adenin, guanin, sarcin or hypoxanthin), which are closely allied chemically to caffeine or theobromine. All the organs elaborate the acid, but nuclear organs, such as the spleen or lymph-nodes, yield more than muscle-tissue.

The daily amount of uric acid excreted is usually very small (0.2-1.5 gme.), and thus forms only a small part of the total nitrogen. Animal food generally causes a considerable increase, but the relation which the elimination of uric acid bears to disease is still imperfectly understood.

In gout a diminution is generally noted before the attack, and an increase directly after; but abnormal figures are found in so many normal conditions that only the continuous increase would speak for a gouty diathesis. An excessive amount is more constant in the various leukemias, owing to the active disintegration of leucocytes, and in some febrile diseases terminating by crisis, while a diminution sometimes occurs in diabetes and anemia.

Kreatinin.—Kreatinin is derived from kreatin, a substance found in muscle, and is excreted in amounts of about 1 gramme daily. More than this would signify an increased breaking down of muscle-tissue, provided the patient is not upon a strict meat diet.

Since the change of kreatin into kreatinin occurs in the kidneys, a diminution of the latter substance is to be looked for in advanced chronic parenchymatous nephritis. Other conditions sometimes accompanied by a diminution are anemia, phthisis and the muscular atrophies. Chemically, kreatinin is closely allied to guanidin and glycocoll.

Hippuric Acid.—Salts of hippuric acid are constantly present in normal urine, though only in very small quantities (0.1-1.0 gramme daily). Chemically, hippuric acid is benzoyl-amido-acetic acid; it is the only known amido-acid voided normally with the urine. Its nitrogen corresponds to 2.89 per cent. of the total nitrogen, according to Landau. It is now generally assumed

FIG. 15.

Hippuric acid crystals. (Simon.)

that hippuric acid results from the synthesis in the kidneys of benzoic acid and glycocoll, both of which are derived from products of intestinal putrefaction. An excess may be expected after the ingestion of fruits rich in benzoic acid and in acute fevers, diseases of the liver and diabetes mellitus; a diminution in chronic parenchymatous nephritis and amyloid degeneration of the kidneys.

Xanthin (Purin or Alloxur) Bodies.—The chief representatives of these are xanthin, heteroxanthin, paroxanthin, guanin and adenin. Xanthin is the only one which occurs in appreciable quantities, and it is, furthermore, of importance in that it rarely may be the principal constituent of renal stones. Collectively, the purin bodies amount to about 10 per cent. of the uric acid present, and their nitrogen forms 1 per cent. of the total nitrogen. Since

mother substances of uric acid, they are generally increased and diminished under the same conditions as this.

Oxalic and Oxaluric Acids.—The origin of oxalic and oxaluric acids is still in dispute. According to some, they are derived from the uric acid by a process of oxidation; according to others, the connective tissue of the ingested food forms the main source.

There are a large number of vegetables (carrots, tomatoes, spinach, rhubarb, figs, plums, coffee and strawberries) which contain a considerable percentage of the acid, and under certain conditions it may be formed from ingested carbohydrates. The normal daily amount is usually below 0.01 gramme, but in some cases of neurasthenia associated with hyperchlorhydria this amount is considerably increased (oxalic acid diathesis), for unknown reasons. Variations have also been described in a number of other diseases, but these are unimportant, since not constant.

Ferments.—Passing mention may be made of the fact that every normal urine contains traces of a ferment, which is nothing but pepsin secreted by the stomach and excreted by the kidneys.

Pigments.—Every normal urine contains some pigments which impart to it the yellow color. The most important of these are urochrome, also called normal urobilin, and uroerythrin. The former is indirectly derived from the blood, hence is increased in amount when an absorption of a large amount of blood is taking place and diminished when there is a new formation of red corpuscles. Uroerythrin is the pigment which colors uric acid crystals and uratic deposits. It is closely related to hemoglobin, and is said to be increased in hepatic disease.

There are also present in normal urines certain bodies which, though colorless, are readily converted into pigments, and are hence called chromogens. The most important of these is indican, the sodium or potassium indoxyl sulphate, obtained by the union of the indol of intestinal putrefaction with sulphuric acid, and the corresponding skatoxyl salts. Normally, only faint traces are excreted (about 6-7 milligrams in a litre of urine), but in the following conditions there is a decided increase: Auchlorhydria and hypochlorhydria, especially in carcinoma of the stomach; occasionally in the hypersecretion associated with ulcer; in obstruction involving the small intestines, and wherever proteid decomposition is going on in the body, as in empyema, putrid bronchitis and gangrene of the lung.

The tests for indican depend upon its oxidation to indigo-blue.

Phenol.—Found in traces in health, and in larger quantities whenever a decomposition of proteids is going on in the body and after the ingestion of phenol (carbolic acid) or its derivatives. Its significance is, in the main, the same as that of indican and skatol. Differential diagnosis may be assisted by the fact that phenol is often absent in typhoid fever, but present in tuberculous meningitis.

Other Organic Bodies.—About 10 per cent. of the sulphur excreted (neutral sulphur) is found in certain organic compounds, chief among which are the sulphocyanides, derived from the saliva swallowed, and the closely allied cysteïn. Possibly tauro-carbaminic acid is also a normal constituent of human urine.

The property of almost every normal urine to turn the ray of polarized light to the left is due to the presence of small amounts of combined glycuronic acid (see next chapter).

Chlorides.—Next to urea, the substance occurring most abundantly in urine is chloride of sodium (about 15 grammes daily). The chlorine, combined with potassium, ammonium, calcium and magnesium, is much smaller in amount, and it is customary to express the total chlorine in terms of sodium. It is almost entirely derived from the food, since more is ingested than is required by the body.

A marked diminution of chlorides is common to febrile disorders and acute and chronic renal disease. It was formerly considered pathognomonic for lobar pneumonia, but closer investigation showed that the urine of all other conditions associated with marked rise of temperature, with the possible exception of malaria, is poor in salt. A decrease is also observed in various gastric disorders (cancer, dilatation, ulcer), anemia and some mental diseases. An increase may be associated with all conditions in which retention has previously occurred, and during the resorption of exudates and transudates. From a prognostic point of view, a very marked diminution of chlorides during fevers (0.05 gme. daily) points to extreme gravity, while an increase from day to day speaks for an improvement. An idea of the digestive functions of the patient may also be obtained, it being the rule that with 10-15 grammes daily the digestive power is normal.

Sulphates.—Sulphates in the urine are derived chiefly from the decomposition of the proteid material of the body, and only to a slight extent from the sulphates actually ingested. They occur either as mineral sulphates (preformed sulphates) or in combination with certain organic radicals derived from intestinal decom-

position, chief among which are phenol, indoxyl and skatoxyl (conjugate or ethereal sulphates). The normal amount for the total sulphates in twenty-four hours is about 2 or 3 grammes, while the relation of preformed to conjugate sulphates is as 10 to 1. It is thus natural that an excessive amount of sulphates is excreted wherever tissue metabolism is stimulated, as in acute fevers or where there is much intestinal putrefaction, as in coprostasis. The determination of the conjugate sulphates does not, however, offer as valuable an index as that of indican, since only the aromatic part of the proteid molecule is concerned in their excretion. An increase has also been noted in a number of other diseases, such as leukemia, diabetes and progressive muscular atrophy, while the conjugate sulphates alone may be abundant in diminished secretion of gastric juice and in obstructive jaundice. Subnormal figures are commonly seen with chronic renal disease and during convalescence from fevers.

Phosphates.—Since phosphoric acid occurs in the urine in combination with potassium, sodium, calcium and magnesium, and the acid itself is tribasic, twelve different combinations are possible. In addition, a small amount is usually found combined with glycerine, as glycerino-phosphoric acid. The most important salt is the diacid sodium phosphate (NaH_2PO_4), to which the acidity of the urine is due; but in case the urine voided is amphoteric or alkaline in reaction, the more basic compounds are in excess. The normal amount of phosphoric acid excreted is about 2.5 grammes. Its source is the food ingested, and to a less degree the disintegrated proteid molecule of the tissues. A diminished excretion is noted in acute fevers, kidney and bone disease; an increased elimination in the so-called phosphatic diabetes and during convalescence from acute fevers.

Nitrates, carbonates and iron salts occur in the urine in mere traces, and their excretion bears no definite relation to any disease. They are chiefly derived from food ingested, the nitrates and carbonates, or salts readily breaking up into carbonates, being abundant in vegetables and fruits, and iron in vegetables and muscle tissue. The estimation of sodium, potassium, calcium and magnesium is of little value. Ammonia normally constitutes about 4.1-4.7 per cent. of the total nitrogen present; that is, it is excreted to the extent of about 0.7 gramme daily. It is present in combination with various acids, and suffers an increase with extensive parenchymatous degeneration, such as acute yellow atrophy and phosphorus poisoning, in respiratory dyspnea and diabetes mellitus.

CHAPTER IV.

THE ABNORMAL CONSTITUENTS OF THE URINE AND THEIR SIGNIFICANCE.

The following substances may occur in the urine during disease:

Albumin . .	Serum albumin.	Hemoglobin.
	Serum globulin	Melanin.
	Albumose.	Bile-pigments.
	Peptone.	Bile acids.
	Bence-Jones albumin.	Urobilin.
	Fibrin.	Fats.
	Nucleoalbumin.	Cholestrin.
	Mucin.	Leucin.
	Histon.	Tyrosin.
	Nucleohiston.	Cystin.
Sugar . . .	Glucose.	Alkapton
	Lactose.	Chromogens responsible for the diazo and dimethylamidobenzaldehyde reaction.
	Maltose.	
	Levulose.	
	Laiose.	
	Pentose.	
	Glycuronic Acid.	Lactic acid.
Acetone.		Oxyamygdalic acid.
Diacetic Acid.		Volatile acids.
β-Oxybutyric acid.		Ptomaines.
		Hydrogen sulphide.
		Drugs.

Albumin.—Though minute traces of albumin may be found in every normal urine if large quantities are examined by special chemical methods, the detection of even traces by the ordinary reagents is probably always pathological. An exception must, however, be made in case of female urines spontaneously voided. These almost always contain minute quantities, owing to admixture with vaginal secretion.

The most common and important albumin occurring in urine is serum albumin. This is soluble in water, dilute solutions of salt and concentrated solutions of sodium chloride and magnesium sulphate, but is precipitated by ammonium sulphate and by heating up to 72-75° C. Concentrated acids change it into acid albumin, which is soluble in acetic acid, while alkalies convert it into alkali albumin.

Serum globulin is insoluble in water and concentrated solutions of chloride of sodium, sulphate of magnesium and sulphate of ammonium. It is coagulated at about the same temperature as serum albumin.

The presence of serum albumin and serum globulin in the urine is termed albuminuria. This albuminuria may be renal where the abnormal condition depends upon some lesion in the kidney cells, or accidental where there is an admixture of albuminous exudate, blood or lymph from the lower genito-urinary tract. Renal albuminuria, as a rule, signifies that the cells of the glomeruli and the convoluted tubules are so altered that they permit the albumin of the blood to pass through. Hence we find appreciable quantities of albumin in all forms of acute and chronic degeneration, congestion and inflammation of the kidneys. An exception is only seen in certain forms of chronic interstitial nephritis, where the low specific gravity and the presence of various forms of casts alone point to a pathological renal condition. There is, however, another form of renal albuminuria, often wrongly termed physiological albuminuria, which is often noticed in young individuals at certain times of the day or at certain regular periods. While its pathology and significance are not as yet clearly understood, it must be looked upon as a decidedly abnormal condition. At times it is brought on by a cold bath or severe muscular exertion; sometimes it disappears with rest in bed, to make its reappearance as soon as the patient is up and about (orthostatic albuminuria). Casts are frequently absent, and the subjective symptoms beyond those of a concomitant anemia are slight. Recently, however, it has been shown that there are often slight cardiac changes.

Accidental albuminuria is generally due to the addition of albuminous material, such as blood, lymph or semen in the bladder or urethra. Blood, pus, etc., may also come from the kidney or renal pelvis when the term accidental renal albuminuria is used.

While the term "albumin in the urine" generally signifies both serum albumin and serum globulin, appreciable quantities of the latter are only noticed in amyloid degeneration.

Albumoses are intermediary products, formed by the conversion of albumin into peptone by ferments. Three varieties are recognized: protalbumoses, soluble in water and precipitated by saturating with chloride of sodium or sulphate of magnesium; heteroalbumoses, insoluble in water, soluble in physiological salt solution and precipitated at 65° C., and deuteroalbumoses, soluble in water and precipitated only by saturating with ammonium sulphate.

Albumosuria is observed wherever there is a large accumulation of pus in the body, and in some diseases of the liver and intestinal tract. Its detection may be of value in distinguishing between epidemic and cerebro-spinal meningitis.

Most text-books state that peptone, in the modern sense of the word, does not occur in urine. Recently, however, Ito[1] has demonstrated its presence in pneumonia, advanced phthisis, ulcer of the stomach and after child-birth.

Over fifty years ago Bence Jones described a peculiar albumin in the urine of cases suffering from multiple myelomata and other tumors of the bones. The recent researches of Magnus-Levy and Simon make it probable, however, that the substance is a true albumin, which differs from other members of the group in that it dissolves in dilute ammonia after precipitation with alcohol. This substance should be looked for in all cases of obscure anemia, especially where pain in the bones is complained of. Its presence does not, however, seem to be absolutely constant[2], for several cases have been reported where the clinical symptoms and autopsy findings were those of myeloma, yet Bence Jones bodies were absent.

Fibrin occurs but rarely, and is generally associated with chyluria or diphtheritic inflammation of the genito-urinary tract. It has also been encountered in hydronephrosis and chronic interstitial nephritis[3]. The fibrinous coagula are either held in suspension or else separate out on standing; sometimes the entire urine is converted into a jelly-like mass.

Other albumins are very rare. Nucleo-albumin is a proteid containing phosphorus, which occurs in minute trace in normal and many pathological urines. Mucin is closely allied to it, but yields proteid and carbohydrate when split up. It forms the delicate cloud so often seen in urines on standing, and is increased in many pathological conditions of the genito-urinary tract. Histon and nucleo-histon have been found in a few cases of leukemia.

Sugar.—Traces of glucose probably occur in every normal urine, but these are so minute that they escape detection with the ordinary tests. The ingestion of a large amount of sugar may lead to the so-called digestive glycosuria, especially in individuals who have a low tolerance for sugar, though they do not necessarily suffer from diabetes. The abnormal excretion of sugar may be

[1] Deutsch. Arch. f. klin. Med., 1901, p. 29.
[2] See S. Jellinek, Virch. Arch., vol. 177, No. 1.
[3] Quincke, Deutsch. Arch. f. klin. Med., vol. 79, Nos. 3 and 4.

divided into simple glycosuria, a temporary condition occurring with some diseases of the nervous system and digestive tract, and after the use of certain drugs; and diabetes mellitus, a separate and distinct constitutional disease. Since there are several degrees of severity of the latter, and the mildest form disappears with diet, care should be taken to examine the urine voided after some saccharine articles have been ingested before passing a definite opinion. In doubtful cases the patient should be instructed to take a hundred grammes of glucose, as this quantity does not cause glycosuria in health.

The urine of true diabetics may contain from a trace to as much as 10 per cent. of glucose.

The color is generally pale, the specific gravity more than 1,025 and the urea often above normal. It is important to note that the percentage of sugar present only rarely indicates the gravity of the case. A patient may excrete 5 or 6 per cent., and with proper diet his urine may become perfectly normal, while in another case the most careful selection of food will not cause the disappearance of a trace. The prognosis is also modified considerably by the presence of other bodies, such as acetone and diacetic acid.

The relation of diabetes to pancreatic disease is still unsettled. In many of the severer cases advanced pancreatic disease is found at autopsy. Above all, the specific elements of the pancreas, the islands of Langerhaus, are destroyed. Yet there are many cases of grave diabetes where even microscopical examination of the organ fails to detect any change.

The form of diabetes following the experimental injection of phloridzine is of special interest, since this drug seems to harm the renal cells directly, so that appreciable amounts of sugar are filtered from the blood.

Compared with glucose, the other sugars play a very subordinate rôle. Lactose, or sugar of milk, is sometimes seen toward the end of gestation, and in nursing women with excess of milk in their breasts. It may be artificially induced by giving over 120 grammes by mouth. Levulose may occur in conjunction with glucose in diabetes or independently. An important observation concerning this sugar has been made by Strauss.[1] He found that if 100 grammes of levulose and 500 grammes of water are given on an empty stomach to a patient suffering from hepatic disease, the urine collected during the following four hours will almost always contain levulose. Where the liver was normal, levulose appeared

[1] Strauss, Deutsch. med. Woch., 1901.

in only a small percentage. Chajes[1] has examined a large number of cases, and finds levulosuria in hepatic disease in 86.9 per cent.; in other disorders in only 15 per cent.

Levulosuria under other conditions seems to be exceedingly rare. Thus Schlesinger[2] speaks of only five recorded cases where this sugar was voided spontaneously. One patient suffered from transverse myelitis, and the levulose was discovered by accident, while in the others typical diabetic symptoms were present. The family history showed diabetes on the maternal side in two. Obesity was a concomitant symptom in two, while the fifth was suffering from extreme nervousness. The excretion of levulose was very slight in all but one. In two cases dextrose was also voided.

Maltose and laiose may also occur in diabetes, and the former has been met with in several cases of pancreatic disease. Various pentoses (rhamnose, xylose, arabinose) sometimes occur in urine, and are of no significance except that their presence has occasionally led to the wrong diagnosis of diabetes.

Two bodies closely allied to sugar are glycuronic acid and inosit. The former is chemically a pentose-carbonic acid, and is intermediary in its constitution between pentose and hexose. It is never found free in the urine, but always combined with indol and phenol, or with certain drugs (menthol, turpentine, chloral, morphine). According to P. Mayer, glycuronic acid must be regarded as a product of the incomplete combustion of sugar, and is often found in the urine of diabetics who have improved so much that their power of oxidizing sugar is partially restored. It has also been observed after poisoning with curare and acetone.

Inosite is sometimes found when much water is ingested.

Acetone.—Acetone is generally considered to be a decomposition product of albumin, which may occur in traces in normal urine, especially after a purely proteid diet. Larger quantities are found in severe fevers, with much breaking down of proteid tissue; in the cachexias of malignant tumors, and in diabetes. Whenever sugar is detected in urine, the acetone test should be done, as an appreciable quantity may signify an approaching coma. It will often be possible to avert this and to cause a disappearance of the acetone by adding carbohydrates to the diet. Acetonuria has also been observed in certain psychical and intestinal diseases.

Diacetic Acid.—Diacetic acid has the same significance, and

[1] Chajes. Deutsch. med. Woch., May 5, 1904.
[2] Arch. f. exp. Path. u. Pharmak., 1903.

occurs under the same conditions as acetone. It is probably never found in health.

β-Oxybutyric Acid.—β-oxybutyric acid[1] is closely allied chemically to acetone and diacetic acid. If present in amounts of 20.0 grammes or more in the urine, together with an excess of ammonia, diabetic coma is almost certain.

Hemoglobin.—Hemoglobin may occur in the urine in the form of red-blood cells or dissolved. The latter condition is known as hemoglobinuria, and the variety of hemoglobin generally present is methemoglobin. It commonly occurs after the ingestion of certain poisons, notably potassium chlorate and pyrogallic acid, after the transfusion of foreign blood, in extensive burns, and severe infectious diseases, especially malaria. In certain individuals general exposure to cold or the mere immersion of a limb in cold water will be followed by the discharge of bloody urine. Donath believes that the entire process here depends on a hemolytic action of the blood-serum, caused by the presence of serum hemolysins.

Melanin.—In patients suffering from melanotic tumors the urine will sometimes contain a dark-brown pigment or its chromogen, which turns dark after the urine has stood for some time. The detection of melanin is not an absolutely positive sign of melanotic tumor, as similar pigments occur in wasting diseases and malaria. If, however, a melanotic tumor has been extirpated, and melanin appears in the urine later, a metastasis is probable.

Bile Pigments.—Bilirubin is the only bile pigment encountered in urine, but the others may form from bilirubin if the urine has stood for some time. Bilinuria is common to all conditions associated with obstruction of the bile passages, such as catarrhal jaundice, stone of the common duct, cancer and tumors or adhesions of the neighborhood. Bilirubin may also be found in acute yellow atrophy, and sometimes in pernicious anemia, typhoid fever, etc.

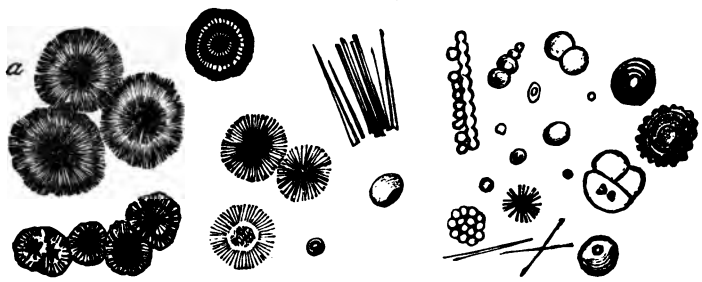
Bile Acids.—Bile acids are found in urine, together with bile pigments, and possess the same significance as these.

Urobilin.—Two forms of urobilin are generally recognized, viz., normal urobilin (urochrome), obtained from the hydrobilirubin eliminated by the intestinal walls, and present in every urine, and the closely allied pathological urobilin. This is found in the urine of fevers and many other conditions, notably pernicious anemia. There may also be some bilirubin, and the patients frequently have a slight icteric hue.

[1] Herter and Richards. Medical News, 1903.

Fats.—Small amounts of fat may occur whenever the renal cells undergo fatty degeneration. Larger quantities render the urine turbid (lipuria), and are seen wherever there is an excess of fat in the blood, as after large doses of oil, in some cases of fracture of

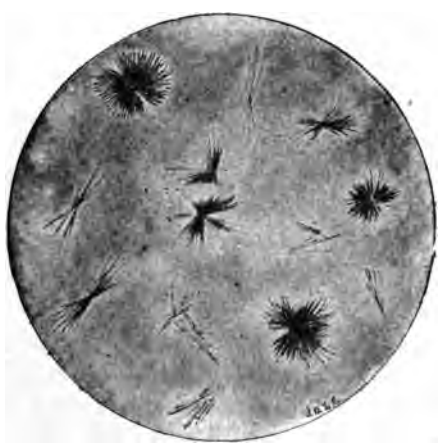
FIG. 16.



Crystals of leucin (different forms). (Crystals of kreatinin chloride of zinc resemble the leucin crystals depicted at *a*.) The crystals figured toward the right consist of comparatively impure leucin. (From Charles: *Chemistry*.)

the bones, diabetes mellitus, eclampsia, etc. In the peculiar condition known as chyluria the fat occurs in emulsified form. It is generally associated with the presence of *filaria sanguinis hominis*

FIG. 17.



Tyrosin crystals. (Musser.)

in the blood. In one case (D. Stürtz) *Eustrongylus gigas* was found, and rarely no parasite is present, but some distinct lesion of the kidney allows the fat to pass through.

Cholesterin.—Though a normal ingredient of bile, cholesterin is usually not found in icteric urine, but in a number of pathological conditions of the genito-urinary tract. The crystals excreted are sometimes very large.

Leucin and Tyrosin.—Both leucin and tyrosin are decomposition products of albumin, and are formed abundantly during pancreatic digestion. They are encountered in the sediment of urines of acute yellow atrophy and other severe hepatic diseases.

Cystin.—Cystin occurs only in exceptional cases in the urine, but is not associated with any definite disease. Like alkaptonuria, cystinuria probably depends upon a localized, specific disturbance in the katabolism of proteids. It is especially of interest in its association with cystin gravel or calculi, but, strangely, the cystinuria may persist for years, even after the stones have been removed. The urine is peculiar in that it is often neutral or alkaline, of a peculiar greenish-yellow color and with a distinct odor of hydrogen sulphide.

Alkaptonuria.—In the peculiar condition known as alkaptonuria the urine turns rapidly brown when exposed to the air and upon the addition of alkalies. Chloride of iron will give a temporary bluish-green color, while ammoniacal silver and Fehling's solution are reduced. It is not difficult, however, to distinguish such urine from diabetic urine, since it does not reduce bismuth, ferment, nor turn the plane of polarized light. The condition is generally congenital; the parents of the patients are often close blood connections, and there seems to be a close relation to that pathological lesion known as ochrinosis. The foreign substance in the urine is homogentisinic, and sometimes uroleucinic acid, whose mother substances are tyrosin and phenylalanin. Abderhalden and Falta found homogentisinic acid in the blood of a case of alkaptonuria. The cause of the disturbance underlying this condition was found to be neither in the intestinal canal nor in the process of absorption.

Diazo Reaction.—In certain febrile diseases, notably typhoid, miliary tuberculosis and measles, a chromogen appears in the urine, which is converted into a red pigment when the urine is treated with certain reagents. This reaction may be of the greatest value in the diagnosis of typhoid fever, since it may appear as early as the fifth or sixth day, when the Widal test is still negative. Simon has examined a large number of cases, and has obtained positive results in 95 per cent. of typhoid cases, in 2 out of 16 cases of pulmonary tuberculosis, 3 out of 4 of septicemia, 2

out of 4 of carcinoma, 1 out of 11 of pneumonia and in all typhoid relapses. In his cases of measles the reaction was not present. It is stated that a diazo occurring in the course of a pulmonary phthisis indicates an extensive process, with grave prognosis.

Dimethylamidobenzaldehyde Reaction.—In 1901 Ehrlich found that in various pathological conditions a cherry-red color will be obtained if the urine is shaken with a few drops of dimethylamidobenzaldehyde in acid solution. The resulting pigment can be extracted with chloroform or dichlorhydrin. With normal urines a reaction also occurs, but much less intense. The occurrence of the reaction is summarized by Simon as follows: A direct reaction of pathological grade does not occur in health. A positive reaction is most commonly obtained in cases of tuberculosis, but may also be seen in non-tuberculous urines, both febrile and non-febrile. It does not depend upon the presence of the body which gives rise to the diazo reaction. For its production, elevation of temperature, gastro-intestinal disturbances and cyanosis are not essential. Common to all cases seems to be an increased katabolism of the tissue albumins.

Pancreatic Reaction.—Mayo Robson and P. J. Cammidge[1] have published their observations and researches on the chemistry of the urine in diseases of the pancreas. They state that the urine here very frequently contains glycerine, and that the glycerine can be easily converted by means of hydrochloric acid into glycerose, which is then precipitated in the form of an osazone with phenylhydrazine hydrochlorate. The authors furthermore state that in some diseases of the pancreas the reaction is prevented by mercuric chloride, while in others this substance does not interfere, and that the size of the crystals and the rapidity with which they dissolve differ for different pathological lesions. J. H. Schroeder[2] states, however, that nitric acid, but not hydrochloric acid, can, under certain conditions, change glycerine into glycerose, and that it is against all laws of physics and chemistry to assume different sizes of the same crystals and different solubility as characteristic of different diseases of the same organ.

Other Organic Principles.—In phosphorus poisoning and acute yellow atrophy of the liver, lactic acid may occasionally be found in the urine. In the latter condition there may also be some oxyamygdalic acid. Volatile acids (formic, acetic, butyric, proprionic) may also occur in febrile conditions and suppurative

[1] Lancet, March 19, 1904.
[2] American Medicine, Sept. 3, 1904.

processes. Rosenfeld[1] believes their amount has some diagnostic significance, since he has found them in ulcer of the stomach and gastrectasy with normal or hyperacidity, and in carcinoma with stagnation and sub or anacidity; while in stagnation due to old pyloric scars, or gastroptosis with sub or anacidity they were diminished. Finally, certain very toxic ptomaines (cadaverin, putrescin) are found in rare instances.

Gases.—Urines containing albumin or cystin will often develop a distinct odor of sulphuretted hydrogen on standing. Sometimes this decomposition already occurs in the bladder in otherwise normal urines, due to the action of certain micro-organisms on the neutral sulphur. The term pneumaturia is generally applied to the discharge of urine containing an appreciable quantity of carbon dioxide, as in diabetes where yeast formation has already taken place in the bladder.

Drugs.—Many of the common remedies appear in the urine, and can be detected with the ordinary tests. The discovery of lead, arsenic or mercury may clear up doubtful cases of poisoning. In addition to these, the following drugs give characteristic reactions: iodides, bromides, chlorate of potassium, the active principle of rhubarb, senna and cascara sagrada, santonine, salicylic acid, antipyrine, phenacetine, copaiba, urotropin, chloroform and carbolic acid. After the prolonged use of sulphonal or trional, the urine may become dark-red in color, owing to the presence of hematoporphyrin.

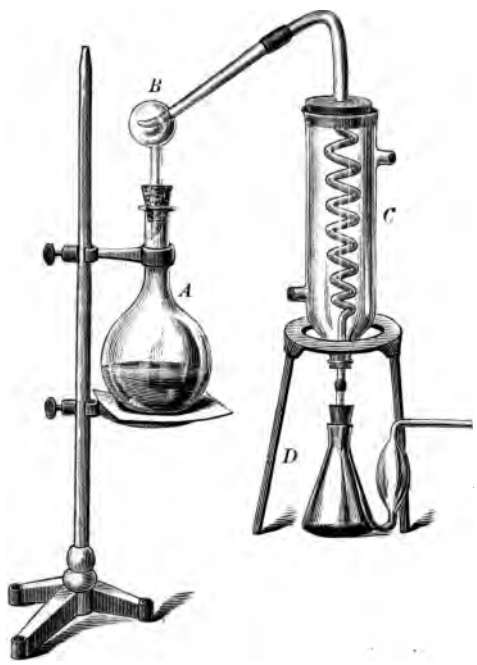
[1] Deutsch. med. Woch., March 26, 1903.

CHAPTER V.

CHEMICAL TESTS FOR NORMAL CONSTITUENTS.

Nitrogenous Principles.—In experimental work it will often be necessary to determine the total nitrogen of urine; that is, the nitrogen yielded by urea, uric acid, the other purin bodies, kreatinin, the amido-acids (chiefly hippuric acid), ammonia and the pigments. In practice, however, a urea estimation will suffice in most cases, since urea forms over four-fifths of the nitrogenous principles present.

FIG. 18.

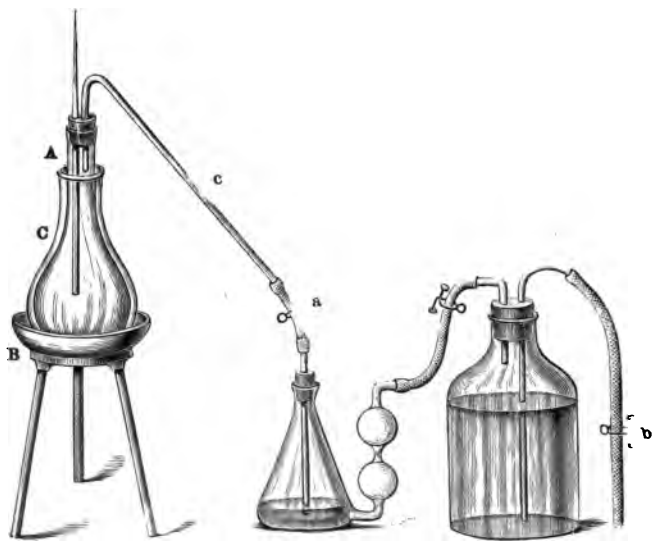


Kjeldahl's nitrogen apparatus. (Simon.)

The method generally employed for determining the total nitrogen is that of Kjeldahl: Ten cubic centimeters of urine are heated on a sand-bath in a flask of hard glass, with ten cubic centimeters of concentrated sulphuric acid and a few drops of copper sulphate solution until the mixture has become colorless or greenish

(about one hour). The flask should be inclined at an angle of 45°, and vigorous ebullition should be avoided. This procedure will convert all the nitrogenous principles into ammonium sulphate. The flask is now connected with a distilling apparatus, and the contents distilled into another flask containing twenty cubic centimeters of half-normal oxalic or sulphuric acid, after the addition of forty cubic centimeters of soda lye of a specific gravity of 1.34. The distillation is interrupted when crystals of sodium sulphate begin to appear, or when about two-thirds of the solution has passed over. After the addition of a few drops of rosolic acid

FIG. 19.



Apparatus for the determination of nitrogen. (Simon.)

solution, the distillate is then titrated with half-normal sodium hydrate solution until the liquid remains red. The amount of nitrogen contained in ten cubic centimeters of urine is obtained by subtracting the number of cubic centimeters of soda solution employed from the amount of half-normal acid in the flask and multiplying the result by 0.007.

Instead of sulphuric acid and copper sulphate, Gunning's mixture may be employed. This consists of 15 c.c. of concentrated sulphuric acid, 10 grammes of potassium sulphate and 0.5 gramme of copper sulphate.

Since difficulty may be experienced in properly heating the urine

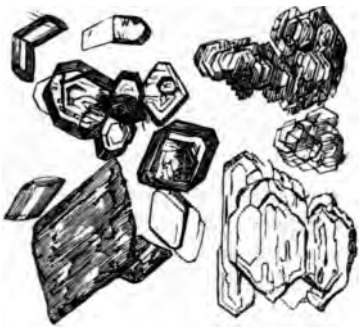
with the sulphuric acid, the method of Will-Varrentrapp may be substituted, since it gives equally as accurate results. Ten c.c. of normal sulphuric acid, together with a few cubic centimeters of a 1 per cent. alcohol phenolphthalein solution, are placed in a Will-Varrentrapp apparatus. Another flask on a sand-bath is filled one-half with dried soda-lime, protected with a hood, and then 5 cubic centimeters of urine permitted to flow in. The two flasks are connected by means of a glass and a rubber tube, which is provided with a stop-cock. The latter is now opened and the urine and soda-lime heated over the sand-bath for one-half to three-quarters of an hour. All nitrogenous principles will be decomposed by the heat and soda-lime into ammonia, which then distils over into the acid. As soon as the heating is discontinued, the Will-Varrentrapp apparatus is connected with an aspirating bottle and air allowed to pass slowly through the entire system for fifteen minutes. The acid is finally titrated with normal sodium hydrate solution until the phenolphthalein turns red. The number of c.c. of solution employed is deducted from 10; the result multiplied by 20, which will give the number of c.c. required to neutralize the ammonia from 100 c.c. of urine. The percentage of nitrogen is then calculated by multiplying by 0.014, but by 0.03 if desired in terms of urea.

Whenever it is desired to ascertain the general distribution of nitrogen in the urine, the total nitrogen is first estimated according to Kjeldahl: A portion of the urine is then precipitated with phosphowolframic acid, and the nitrogen determined in this precipitate; this corresponds to ammonia, the purin bodies, kreatinin and the pigments. The nitrogen in the filtrate will give the figures for urea and the amido-acids. The urea itself is best determined according to Mörner and Sjöquist (v. i.), the purin bodies after Arnstein's modification of Camerer's method (v. i.) and the ammonia according to Folin or Schlosing. The following average figures were obtained during health by A. Landau: Purin nitrogen, 1.01 per cent.; ammonia nitrogen, 2.42 per cent.; urea nitrogen, 90.87 per cent.; amido-acid nitrogen, 2.89 per cent.

Urea.—If it is desired to demonstrate the presence of urea in a fluid, as in the vomitus or serum of uremia, etc., 20-25 cubic centimeters are evaporated in a porcelain dish upon a water-bath to a thin syrup. Upon the addition of several cubic centimeters of concentrated nitric acid, nitrate of urea will crystallize out, which can be identified under the microscope as typical, superimposed, rhombic plates. By decomposing the salt with carbonate of

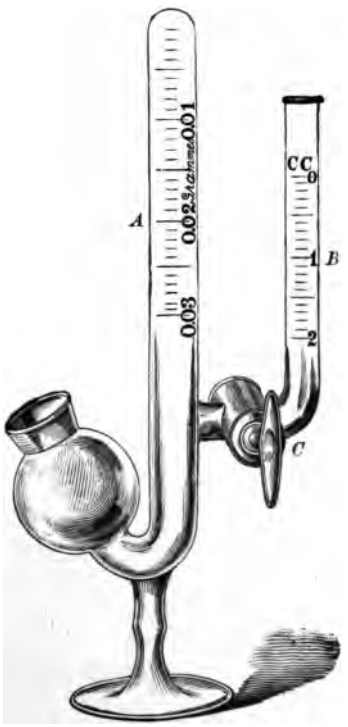
barium, pure urea may be obtained, which will give the biuret reaction.

FIG. 20.



Urea nitrate crystals. (Krukenburg, after Kühne.)

FIG. 21.



Doremus' ureometer.

For the quantitative determination of urea, the method of Doremus is most convenient. A tube, consisting of a long, closed

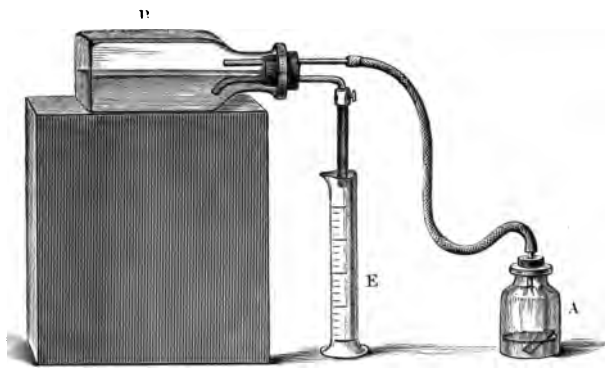
arm and a short, wide, open one, is filled with a solution of hypobromite of sodium, made by mixing 5 cubic centimeters of bromine, 70 cubic centimeters of a 30 per cent. by volume solution of sodium hydrate and 180 cubic centimeters of water. The solution should not be kept more than a few days. One cubic centimeter of urine is then passed into the long arm by means of a specially-constructed pipette. The hypobromite will decompose the urea into carbon dioxide, water and nitrogen; the carbon dioxide is absorbed by the excess of alkali present, while the nitrogen is set free, and its volume can be read off in terms of urea. In a later model of Doremus a graduated tube projects from the long arm, which takes the place of the pipette. In albuminous urines considerable frothing occurs, and it is always better to remove the albumin. While this method is but a crude one, it is sufficiently accurate for ordinary clinical work, especially if the urine is diluted, should it contain more than 1 per cent. of urea. The temperature and barometric pressure need not be taken into account, but at least half an hour should elapse before the reading is taken.

The apparatus which Simon[1] recommends, although also a volumetric one, gives much more accurate results. It consists of a burette C, with an ascending rubber tube attached to the reservoir B, which can be raised or lowered, as required. A descending tube leads to a wide-mouth bottle A, which contains the hypobromite solution. This is closed by a tightly-fitting stopper, to which a loop of platinum wire is attached, carrying a little glass bucket; this can be swung from its support by tilting the bottle. After the stopper is removed from A, water is poured into B until the water level is visible above the point where the rubber tube is adjusted. About 25-30 c.c. of hypobromite solution are placed in the bottle A, and 2 c.c. of urine accurately measured into the bucket. The stopper is carefully adjusted, the water in B and C brought to the same level and the reading taken. The bucket is now dropped into the hypobromite solution by inclining A. The liberated nitrogen will collect in the burette and depress the level of the fluid, when, after twenty or thirty minutes, the pressure in C is equalized by lowering B until the water in both tubes occupies the same level, when the second reading is taken. The difference corresponds to the volume of nitrogen evolved from 2 c.c. of urine. To determine the percentage of urea, this figure must be divided by 354.3 and multiplied by 50. A table must be consulted to correct for temperature and barometric pressure.

[1] Clinical Diagnosis.

Other ureometers are Green's, Marshall's, Hueffner's and Squibb's. Only the last mentioned possesses advantages in being a very simple contrivance. It requires two ordinary medicine bottles, A and B. B is closed by a doubly-perforated rubber stopper, a straight tube passing through the upper aperture and connecting with A, in which the nitrogen is evolved out of 25 c.c. of hypobromite solution and 2 c.c. of urine, which latter is contained in a small tube. Another tube, bent downward and carrying a clamp, passes through the lower aperture, and leads to a graduated cylinder. B contains just enough water for the bent tube to dip in. The clamp is opened, and the urine and solution mixed by inclining A. The nitrogen, as it escapes into B, will displace its volume of water, which flows into E, and can be readily measured. A table will then give the amount of urea.

FIG. 22.



Squibb's ureometer.

In Folin's[1] recent method urea is decomposed into ammonia and carbon dioxide by a concentrated solution of magnesium chloride.

A very novel test is that of Miguel.[2] It is well known that urea is decomposed into carbonate of ammonia on standing, through the agency of micro-organisms. A ferment is isolated from the latter and dissolved to a clear solution. Equal quantities of this and of urine are mixed, and the ammonia determined at once, and after the mixture has been digested for two hours at 50° C. By subtracting the first from the second determination, the amount of ammonia corresponding to the urea present may be easily determined.

[1] Zeitsch. f. physiol. Chemie, vol. 22, p. 504, and vol. 36. p. 333.
[2] Comptes Rendues., 1890.

PLATE I.

FIG. 1.

Uric Acid. (Musser.)

A. Common forms. *B*. Amorphous urates

(Ob. D. and A., Oc. 4.) Drawn by J. D. Z. Chase

FIG. 2.

Combination of Uric Acid and Calcium Oxalate. (Musser.)

(Oc. 4, Ob. D.) Drawn by J. D. Z. Chase.

For more accurate work, Mörner and Sjöquist have devised the following method: Five c.c. of urine and 5 c.c. of a mixture containing 10 grammes of chloride of barium and 3-4 grammes of caustic baryta to 100 c.c. of water are mixed in a flask with 100 c.c. of an alcohol-ether mixture (alcohol, 97 per cent., 2 volume; ether, 1 volume), allowed to stand until the next day, filtered, washed with the alcohol-ether mixture and then evaporated with gentle heat. As soon as the volume has reached about 25 c.c., some water and milk of magnesia (magnesia usta 1, water 12) are added, and the whole heated until the vapor no longer reacts alkaline. The fluid and precipitate are washed into a flask with the aid of some dilute sulphuric acid, and the nitrogen then determined according to Kjeldahl.

Uric Acid.—Fifty to 100 c.c. of urine are strongly acidified by the addition of hydrochloric acid, when the uric acid will crystallize out after several hours in the form of yellowish-brown crystals. These crystals are collected on a filter, washed with water and then transferred to a porcelain dish. If they are now heated carefully with two or three drops of concentrated nitric acid until the acid has evaporated, the addition of a few drops of ammonia will give rise to a purple color; of potash lye, to a violet color (murexid test). On warming, the color will disappear rapidly (difference from xanthin bodies).

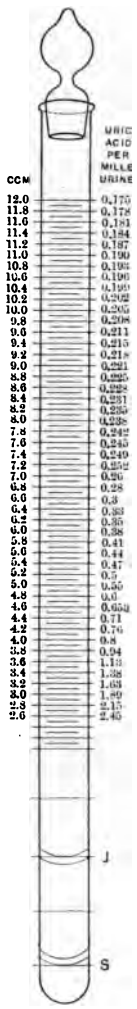
Tichborne[1] has modified the test as follows: Some nitric acid is added to urine, and the whole evaporated on the water-bath. Circular bands of uric acid will form in the dish, and at one place the concentration of nitric acid will be just sufficient to bring about a purple color when the dish is held over ammonia water.

For quantitative analysis the following method is recommended (Hopkins): Fifty c.c. of urine are rendered faintly alkaline with ammonia and gently warmed to about 40° C. Fifteen grammes of powdered ammonium chloride are then added, and the mixture set aside. At the end of two hours all the uric acid will have precipitated in the form of its ammonium salt. The urine is then filtered, and the precipitate washed with a saturated solution of ammonium sulphate until the filtrate no longer gives a precipitate with silver nitrate. The filter-paper is then punctured, and the ammonium urate washed into a clean flask with the aid of some boiling distilled water. The salt is decomposed with 7 to 8 cubic centimeters of concentrated sulphuric acid, and the amount of uric acid finally determined by titrating with a twentieth-normal

[1] Monatsbl. f. prakt Dermatol, 1888.

solution of potassium permanganate (containing 1.576 grammes per litre) until the pink color persists for at least thirty seconds. Each cubic centimeter of the reagent corresponds to 0.00375 gramme of uric acid. A final correction of 0.0003 gramme for each 100 c.c. of urine is necessary.

FIG. 23.



Ruhemann's uricometer.

Folin's method is still more accurate—75 c.c. of a reagent, consisting of 500 grammes of ammonium sulphate and 5 grammes of uranium acetate dissolved in 650 c.c. of water, with the addition of 60 c.c. of a 10 per cent. solution of acetic acid, are added to 300 c.c. of urine. The mixture is filtered after five minutes, and the filtrate divided into two portions of 125 c.c., each of which is treated with 5 c.c. of concentrated ammonia and set aside until the next day. The precipitated ammonium urate is then filtered off, washed with ammonium sulphate and treated as before.

Instead of adding sulphuric acid and titrating with potassium permanganate, hydrochloric acid may be added to the ammonium urate solution, and the acid not used in decomposing the salt retitrated with sodium hydrate. Or else hydrochloric acid is added to the ammonium urate, the solution then evaporated and the crystals dried and weighed. Haycraft precipitates the uric acid with ammoniacal silver solution and magnesia mixture, and determines the amount of silver by titrating with potassium sulphocyanide. This, however, will also throw down the purin bases.

Although these methods are accurate, they are rather troublesome, and consume considerable time. Ruhemann has recently constructed a uricometer, which permits of a rapid estimation and is fairly exact. A long, cylindrical tube is filled up to certain marks with carbon disulphide, and then with a solution containing iodine 1.5 grammes, potassium iodide 1.5 gmes. and absolute alcohol 15 grammes in 185 c.c. of distilled water. On adding a certain amount of urine and shaking, the carbon disulphide will become of a dark brown copper color; with more urine the carbon disulphide will absorb all free iodine, and the mixture will look like urine. The adding

of urine should be stopped as soon as the carbon disulphide shows only a slight reddish tint, because this will disappear entirely after repeated shakings. The test is finished when the indicator appears snow-white, a sign that all iodine has been neutralized by the urine. After the foam has settled, the proportion of uric acid is read off on a scale. While very convenient, the end reaction is rather indefinite, and requires considerable experience.

A recent method of uric acid determination is that by J. Rudisch and F. Kleeberg. Like other methods, it is based upon the fact that uric acid and the purin bases form a definite compound with silver in an ammoniacal solution of the latter in the presence of neutral salts of the alkaline and alkaline earth groups, preferably chloride of magnesium, lithium or ammonium. Uric acid will combine with silver in the proportion of one molecule of the former with one atom of the latter; the purin bases in the proportion of two molecules of xanthin to one of silver. The silver urate is insoluble in strong ammonia, but the silver-purin salts are rapidly soluble. The solutions necessary are (1) a fiftieth-normal solution of silver nitrate, made by dissolving 3.3932 grammes silver nitrate previously heated to 120° C. for ten minutes in water, adding 75 c.c. ammonia of specific gravity 0.90 and 10 grammes chloride of ammonia and diluting to one litre; (2) a fiftieth-normal potassium iodide solution, prepared by dissolving 3.32 grammes potassium iodide in a litre of water; (3) a nitrous-sulphuric acid mixture, prepared by adding 25 c.c. concentrated sulphuric acid to 75 c.c. of water, and then adding 1 c.c. fuming nitric acid; (4) a starch solution, and (5) ammonia water of specific gravity 0.90. In order to determine the amount of uric acid, 55 c.c. of silver solution are added to 110 c.c. of urine, and the whole diluted up to 220 c.c. with ammonia. After filtering two portions of 100 c.c., each are collected. In the meantime half a dozen small test-tubes are filled for about 1 centimeter with a mixture of roughly, two parts of nitrous sulphuric acid and one part of starch solution. To one of the portions of 100 c.c., iodide of potash solution is rapidly added, and after every addition of 2 c.c. a small amount is removed by means of a pipette and floated on the solution contained in the test-tube. The end reaction will manifest itself by the appearance of a blue ring, owing to the formation of iodide of starch. The exact end reaction is now determined with the second 100 c.c.; that is, if more than 10 c.c. and less than 12 c.c. are employed in the first determination, 10 c.c. are run in at once; then a few drops are carefully added until the exact point is reached.

In order to determine the purin bases, the same process is carried out, except that water, instead of ammonia, is used to dilute the urine plus silver nitrate solution. The final calculation is as follows: 0.3 c.c. is subtracted from the number of c.c. of iodide solution used, for correction; the resulting number of c.c. is then subtracted from the number of c.c. of silver nitrate solution employed. This figure multiplied by 0.00336 will give the amount of uric acid in 50 c.c. of urine. Thus, if 15.9 c.c. of iodide solution have been used for 100 c.c. urine mixture, 15.9 — 0.3 = 15.6; 25 (the number of c.c. of silver solution in 100 c.c. mixture) — 15.6 = 9.4; 9.4 × 0.00336 = 0.0316 gramme uric acid in 50 c.c. of urine. For purin bases the number of c.c. corresponding to uric acid, previously determined, are subtracted from the new figure obtained and the result multiplied by 0.00152. Thus, if 14.2 c.c. iodide solution are used for 100 c.c. mixture, 14.2 — 0.3 (the correction) = 13.9; 25 (the amount of silver solution contained in 100 c.c. mixture) — 13.9 = 11.1; 11.1 — 9.4 (the figure previously obtained for uric acid) = 1.7; 1.7 × 0.00152 = 0.0026 grammes of purin bodies, in terms of xanthin, contained in 50 c.c. of urine.

The following precautions are mentioned by the authors: (1) In making the test for iodine, the solutions should be absolutely cold, and it is preferable to place the test-tubes in ice-water. (2) The end reaction can be observed most accurately in daylight. (3) Many urines, if added to the nitrous-sulphuric mixture, will develop a reddish-colored ring at the point of contact. This color is due to the action of the acid on the coloring matter of the urine, and is noticed only when working with the weak ammoniacal solution. If doubt exists as to the nature of the ring, it is only necessary to gently shake the test-tube, without causing the liquids to mix completely. Under these conditions the reddish ring disappears entirely, while the blue iodine ring becomes more distinct. (4) If the urine contains a uric acid deposit, this should be dissolved by warming, or by the addition of lithium carbonate. (5) Albumin and sugar do not interfere, but iodide of potassium must be removed by adding silver nitrate in excess, and then a chloride to remove the excess of silver.

The authors have tested their method by control estimations with the Ludwig Salkowski method for uric acid and the Arnstein modification of the Camerer method for purin bases, and have found only slight discrepancies. The writer has had occasion to try the method in two instances, and finds it comparatively simple,

but has had some difficulty in detecting the first appearance of the blue ring.

Purin Bases. Arnstein's[1] Modification of Camerer's Method. —240 c.c. of urine are treated with 30 c.c. of magnesia mixture (crystallized magnesium sulphate, 1; chloride of ammonia, 2; ammonia water, 4; water, 8) and filled up to 300 c.c. with 20 per cent. ammonia. After shaking, the mixture is at once filtered. Two portions of the filtrate, of 125 c.c. each (= 100 c.c. urine), are treated each with 10 c.c. of ammoniacal silver solution (3 per cent silver nitrate, with the addition of some ammonia). The resulting precipitate is filtered with the aid of an air-pump, and washed with 250-300 c.c. of water until free of ammonia. The nitrogen is then determined in the precipitate according to Kjeldahl's method. The urine should be first freed from albumin.

Salkowski's method is preferable in many ways, since a nitrogen determination is not necessary. Five hundred c.c. of urine, free from albumin, are treated with 50 c.c. of magnesia mixture, and filled up to 600 c.c. with strong ammonia and filtered.

To 540 c.c. of the filtrate, 30-35 c.c. of a 30 per cent. aqueous solution of silver nitrate are added. The precipitate, which should be gelatinous, is allowed to stand for an hour, then filtered from the urine, washed and transferred into a flask, acidified with a few drops of hydrochloric acid and split up with sulphuretted hydrogen.

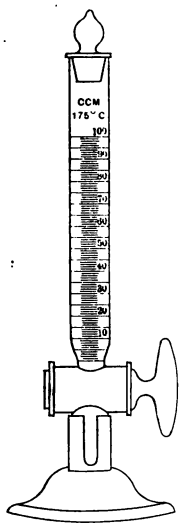
The next steps consist in heating the flask on a water-bath, filtering, washing the precipitate and evaporating the filtrate to dryness. The residue is then heated up to boiling with 25-30 c.c. dilute sulphuric acid. The fluid is permitted to stand sixteen to twenty hours, when the uric acid can be filtered off and washed with dilute acid. The filtrate and washings are then supersaturated with ammonia, precipitated with silver nitrate solution, filtered and washed. The amount of silver is determined by incinerating the precipitate in a platinum crucible, dissolving the ash in nitric acid, titrating with one-fiftieth normal sulphocyanide solution. Each c.c. of this will correspond to 1.52 grammes xanthin.

These complicated methods have been much simplified, and quite recently a very practical purinometer has been placed on the market. It consists of a tall glass cylinder, divided into an upper graduated portion, separated from a lower one by a tap. With the tap at right angles to the tube, 90 c.c. of urine and 20 c.c. of solu-

[1] Zeitsch. f. physiol. Chemie, 1897, p. 426.

tion No. 1 (magnesia mixture) are poured in, and the tap then opened. The phosphates will precipitate at once. In ten minutes they will have passed into the lower portion of the tubes; the tap is again turned at right angles and solution No. 2 (silver nitrate) is added up to 100 c.c. The resultant precipitate of silver-purin should be pale yellow. If some silver chloride has formed, a few drops of ammonia may be added. The apparatus is then kept in a dark place, and after twenty-four hours the number of c.c. occupied by the precipitate may be read off and compared with a table. The result will give percentage of purin nitrogen, inclusive of uric acid.

FIG. 24.



Purinometer.

Personal experience with the purinometer has not been very favorable. It is difficult to read off the height of the precipitate accurately, since this tends to cling to the glass, and control tests with more accurate methods often give discordant results.

Kreatinin. Weyl-Salkowski Test.—A few cubic centimeters of urine are treated with a 5 per cent. solution of sodium nitroprusside, and then with a few drops of sodium hydrate solution. Kreatinin will give rise to a deep red color, which is changed to green on warming with glacial acetic acid. On standing, a deposit of Prussian blue is formed.

The quantitative estimation is conducted as follows: 480 c.c. of urine are rendered alkaline with milk of lime, and then precipitated completely with chloride of calcium. The mixture is then filtered, after enough water had been added to make 600 c.c.; 500 c.c. of the filtrate, which should react faintly alkaline, are evaporated to 40 c.c. on the water-bath, mixed with an equal volume of absolute alcohol, and brought up to 200 c.c. with alcohol. After filtering, 160 c.c. are treated with 1-2 c.c. of an alcoholic solution of chloride of zinc (sp. gr. 1.20). After three or four days the crystals of kreatinin-zinc-chloride are filtered off, dried and weighed. The result, multiplied by 0.6244, will give the amount of kreatinin present.

Amido-Acids.—The only amido-acid normally present which can be estimated quantitatively is hippuric acid. A large quantity of urine is evaporated to syrupy consistence, and then extracted

with alcohol. The alcohol is removed by distillation, the remaining solution acidified with acetic acid and treated with alcoholic ether. The ether is now distilled off, the remaining solution evaporated on a water-bath, the residue boiled with water, cooled and filtered. The filtrate is rendered alkaline with milk of lime, the excess of calcium removed with carbon dioxide. The calcium salts remaining in solution are decomposed with acid, and the solution then extracted with ether, which will dissolve out the hippuric acid. The crystals are dried and weighed after the ether has evaporated. In pathological conditions two other amido-acids—leucin and tyrosin—may occur *(vide infra)*.

Oxalic Acid.—In order to demonstrate the presence of oxalic acid in the urine it is frequently only necessary to examine the sediment, as the crystals are characteristic. Since there may, however, be no crystals, even when large amounts are present in the urine, precipitation must be brought about by carefully neutralizing with ammonia or by treating the urine with one-third its volume of 95 per cent. alcohol and setting aside for twenty-four or forty-eight hours.

For quantitative work, 500 c.c. of urine are evaporated to 150 c.c., and then shaken with 20 c.c. dilute muriatic acid and the same amount of a mixture of ether, nine parts plus alcohol one part, in a separating funnel. The ether is collected in a flask and distilled off, the remainder then heated on a water-bath until all traces of alcohol and ether have disappeared. The remaining fluid is filtered, and rendered alkaline with ammonia. Upon adding 1-2 c.c. 10 per cent. solution of chloride of calcium and acidifying with acetic acid, crystals of oxalate of lime will separate out, and can then be collected on a filter, dried and weighed.

A somewhat better method has recently been recommended by Albahary.[1] Fifty c.c. of a 10 per cent. solution of sodium carbonate are added to the entire urine of twenty-four hours. This is then concentrated on a water-bath to one-third its volume; 20 c.c. of a solution containing 10 per cent. magnesium chloride and 20 per cent. ammonium chloride are added, with some purified animal charcoal, and the mixture further concentrated to one-fourth. The charcoal is removed by filtering, the filtrate rendered strongly alkaline with ammonia and allowed to stand for twelve hours. The mixture is then again filtered, and the filtrate acidified slightly with acetic acid and treated with calcium chloride in excess. After twelve hours the calcium oxalate can be collected

[1] Chemiker Zeitung, 1903, p. 732.

on a filter, dissolved in sulphuric acid and determined by titration with potassium permanganate.

Ferments.—Pepsine can readily be detected in the urine by digesting large quantities of urine with flakes of fibrin. By determining the critical temperature—*i. e.*, the temperature at which digestion will cease—the identity between gastric and urinary ferments can be established.

Urochrome.—In order to obtain urochrome from normal urine, 1-1.5 grammes dilute sulphuric acid are added to the litre of urine, which is then filtered and saturated with ammonium sulphate. The resulting flakes are treated with warm, ammoniacal, absolute alcohol, when the pigment will be obtained on evaporating the alcohol. An alcoholic solution will exhibit a greenish fluorescence when treated with ammonia and zinc chloride.

Klemperer[1] measures the amount of urochrome present in urine by comparing its color with a test solution of echt-gelb (0.1 gramme dissolved in 1 litre of water; 5 c.c. of this diluted up to 90 c.c. with water will correspond to a 0.1 per cent. solution of urochrome). The color of normal urine voided in amounts of 1,500 c.c. in twenty-four hours corresponds to about 0.15 per cent. urochrome. If the amount of urine be diminished by excessive perspiration or diarrhea, the amount of urochrome will correspond to 0.3-0.4 per cent. urochrome. This deep tinge is evidence of sufficient functional activity on the part of the kidneys. In severe renal disease the urine will be less abundant, without being darker in color. It may be stated that the lighter the tinge, the more serious the pathological changes. The color is particularly important in heart disease.

Cardiac weakness, with marked venous stasis, will give dark urine as long as the kidneys are in fair condition. If the urine is light-tinged, the kidneys are beginning to fail, and the prognosis is unfavorable.

Uroerythrin.—When urine is precipitated with lead acetate or barium chloride, a rose color will be imparted to the white precipitate in the presence of uroerythrin. This pigment is very unstable, but readily soluble in amyl alcohol.

Indican.—A few cubic centimeters of urine are treated with an equal amount of Obermayer's reagent (2 pro mille solution of ferric chloride in concentrated hydrochloric acid) and set aside for a few seconds. If the mixture is now shaken with a small amount of chloroform, a distinct blue color will be imparted to the

[1] Berl. klin. Woch., April 6, 1903.

latter in the presence of indican. Instead of Obermayer's reagent, the urine may be mixed with an equal amount of concentrated hydrochloric acid and one or two drops of a strong solution of chlorinated lime. Bile and other pigments must first be removed by means of a solution of subacetate of lead. Riegler employs barium peroxide, which will liberate peroxide of hydrogen in the presence of hydrochloric acid.

In testing for indican, the chloroform will sometimes turn red instead of blue, indicating the presence of skatol, which has the same significance as indican. It is, however, much better removed with amyl alcohol. In other cases the red color will not be taken up with chloroform, and is then due to urorosein (an unimportant pigment) or skatol carbonic acid (detected by adding a few drops of hydrochloric acid and very dilute chloride of iron solution and boiling, when a cherry-red color will appear). In the presence of iodides the chloroform will be tinged violet.

For quantitative analysis, an approximate estimation from the depth of color of the chloroform will generally suffice. For more accurate work, Strauss has constructed a special separating funnel. Twenty c.c. of urine are first treated with 5 c.c. of a 20 per cent. lead acetate solution and filtered. Ten c.c. of the filtrate are shaken with an equal amount of Obermayer's reagent and 5 c.c. of chloroform in the funnel. The chloroform is drawn off, fresh chloroform added and the process repeated until no more indigo is extracted. Two c.c. of the combined extractions are then diluted with chloroform until the color corresponds with that of a standard solution.

Ellinger[1] has recently recommended the following method: The urine, which should be acid in reaction, is treated with one-tenth its volume of liquid plumbi subacetatis and filtered. A given volume of the filtrate is mixed with an equal volume of Obermayer's reagent. The resulting indigo is extracted with successive portions of chloroform by shaking the tube about two minutes after each addition. The volume of the filtrate should be such that not more than about 30 c.c. of chloroform are required. The chloroform extracts are allowed to stand a few minutes, filtered through a dry filter into a dry, perfectly clean flask and evaporated on a water-bath to dryness. The residue is washed two or three times with hot water, and dissolved in 10 c.c. of pure sulphuric acid by heating on the water-bath for five to ten minutes. The solution is then transferred to a flask containing about 100 c.c. of

[1] Zeitsch. f. phys. Chemie, vol. 38, Nos. 1 and 2.

distilled water, and titrated with potassium permanganate solution (5 c.c. of a 0.3 per cent. solution, diluted with 200 c.c. of water) until a clear, yellow color is reached. Each c.c. will correspond to 0.177 milligrams of indigo.

Neutral Sulphur.—In order to determine the amount of neutral sulphur it is first necessary to estimate the total sulphur (A) and then the inorganic sulphur (B), and finally to subtract B from A.

The amount of total sulphur is computed as follows: 100 c.c. of urine are treated with 12 grammes of a mixture of 12 grammes of sodium and potassium carbonate (11 : 14) and evaporated to dryness in a nickel crucible. The residue is fused thoroughly, allowed to cool and extracted with hot water. The residue is filtered off and filtrate and washings treated with a few crystals of potassium permanganate. After heating for about fifteen minutes, concentrated hydrochloric acid is added until the reaction is distinctly acid. The solution is then brought to the boiling point and treated with about 20 c.c. of a saturated solution of barium chloride. Finally the barium sulphate is collected and weighed. The amount multiplied by 0.4206 will give the amount of sulphur in terms of sulphuric acid, by 0.34335 in terms of sulphuric anhydride and by 0.13744 as actual sulphur.

Chlorides.—Chlorides are detected in urine by acidifying with nitric acid and adding a few drops of 10 per cent. solution of silver nitrate. The reaction may be expressed in the following terms: Heavy precipitate, slight precipitate, turbidity, faint turbidity. For ordinary purposes the following method is a fair quantitative test: Ten c.c. of urine are treated with a few drops of potassium chromate solution, and then titrated with a one-tenth normal solution of silver nitrate until a faint orange tint no longer disappears on stirring. Uric acid, the xanthin bases, iodides and bromides will also react with silver nitrate, and if these substances are present in large amounts too high figures will be obtained.

In case iodides and bromides are present, the iodine and bromine should be liberated by the addition of potassium nitrite and sulphuric acid, and then extracted with carbon disulphide. After extraction the nitrous acid is decomposed by the addition of a little urea, and the solution neutralized with sodium carbonate.

Method of Salkowski-Volhard:[1] Ten c.c. of urine are diluted with 50 c.c. of distilled water, and acidified with 4 c.c. of nitric acid. From a burette 15 c.c. of a standard solution of silver

[1] Zeitsch. f. physiol. Chemie, vol. 1, p. 16, and vol. 2, p. 87.

nitrate are then added (29.059 grammes of silver nitrate, previously heated, to 1 litre of water; 1 c.c. = 0.01 gramme of sodium chloride), the mixture thoroughly agitated and diluted with water up to 100 c.c. The resulting silver chloride is removed by filtering through a dry filter into a dry flask. Eighty c.c. of the filtrate are then mixed with 5 c.c. of an ammonia-ferric alum solution (saturated at ordinary temperature), and titrated with sulphocyanide of potash solution (6.6 grammes to 1 litre) until a slight reddish tinge is seen. On multiplying the result by ½ and deducting from 15, the number of grammes of sodium chloride in 100 c.c. of urine will be obtained.

If the proper facilities are at hand, the method of Neubauer and Salkowski[1] is very simple and accurate. Ten c.c. of urine are evaporated to dryness in a platinum crucible, at a temperature slightly below 100° C. (*e. g.*, on a water-bath), after the addition of a little exsiccated carbonate of soda and 4 grammes of nitrate of potassium. The residue is carefully heated at a moderate temperature, to destroy the organic matter, then dissolved in distilled water and neutralized with nitric acid. The chlorides can now be estimated by a simple titration with standard silver nitrate solution. Albumin and sugar should first be removed.

Sulphates.—Preformed sulphates are detected by acidifying a small amount of urine strongly with acetic acid and adding barium chloride, when a cloud of white precipitate will be obtained. Conjugate sulphates are demonstrated by treating 25 c.c. of urine with an equal volume of a solution consisting of two parts of saturated barium hydrate and one part of saturated barium chloride and filtering. In the presence of conjugate sulphates the filtrate will show a precipitate if strongly acidified with hydrochloric acid and boiled.

In order to determine the amount of preformed and conjugate sulphates, the total sulphates are estimated in one portion and the conjugate sulphates in another; the difference between the two gives the preformed sulphates.

Total sulphates are estimated as follows: 100 c.c. of filtered urine are boiled for ten minutes with 10 c.c. of muriatic acid, then mixed with hot chloride of barium solution (10-15 c.c.), and allowed to stand until the next day, when the precipitate is filtered off and washed twice with absolute alcohol and once with ether to remove pigments. The precipitate is heated in a platinum crucible until it appears perfectly white, and finally weighed. For calculation, see under Neutral Sulphur.

[1] Pflüger's Arch., vol. 6, p. 214.

For the quantitative estimation of conjugate sulphates, 100 c.c. of urine are mixed with 100 c.c. of an alkaline solution of barium chloride (see above), and filtered to the 100 c.c. mark. Dilute hydrochloric acid is now added, and the whole boiled until the barium sulphate has settled and the supernatant liquid is clear. The precipitate is filtered off, washed, dried and weighed as above. The weight, multiplied by 2 and deducted from the amount found by the first method, indicates the quantity of preformed sulphates.

Phosphates.—To demonstrate the presence of earthy phosphates, it is only necessary to render the urine alkaline with ammonia, when a flocculent precipitate will occur. To demonstrate alkaline phosphates, the urine is now filtered, acidified with acetic acid treated with a few drops of ferric chloride or uranium nitrate solution or with magnesia mixture, when a white precipitate will form.

For quantitative analysis, 50 c.c. of urine are treated with 5 c.c. acetic acid mixture (sodium acetate 100, glacial acetic acid 30, water to make 1,000), heated to boiling and titrated with a solution of uranium nitrate of such strength that 20 c.c. = 0.1 gramme P_2O_5 (44.78 grammes to the litre). A number of drops of potassium ferrocyanide solution are placed on a porcelain plate. After every addition of uranium solution to the boiling urine a drop of the mixture is mixed with a drop of ferrocyanide on the plate. The end reaction is indicated by the presence of a brown color. By multiplying the number of c.c. used by 0.01, the percentage of phosphates present will be obtained.

In order to determine the alkaline phosphates alone, 200 c.c. of urine are rendered strongly alkaline with ammonia, and set aside for several hours, after which the precipitated earthy phosphates are filtered off, washed with dilute ammonia and transferred to a beaker by perforating the filter and washing with water containing a few drops of acetic acid. They are then dissolved in as little acetic acid as possible, and titrated with uranium solution as above. The difference between the result and the total phosphates will give the earthy phosphates.

Nitrates.—Sodium, potassium, calcium, magnesium and iron are never estimated in the ordinary examination of urine. For details, see text-books on quantitative analysis.

Ammonia.—An excellent method for estimating the amount of ammonia in urine is that of Folin. Ten c.c. of urine are diluted to about 450 c.c., and boiled with about 0.5 gramme of burnt magnesia. The distillate is received into a flask containing

decinormal sulphuric acid for forty-five minutes, into a second flask with acid for another forty-five minutes. The first flask will contain all the alkali obtained from the ammonia plus a small amount from urea. The second flask receives only a small amount from urea, so that by subtracting (b) from (a) correct figures will be obtained. Titration is carried on with alizarin as an indicator.

Schlösing's method: 25 c.c. of urine are placed in a flat dish, on the plate of an exsiccator. Above this dish a smaller one, containing 10 c.c. of a normal solution of sulphuric acid, is placed. Ten cubic centimeters of milk of lime are added to the urine, the bell carefully adjusted, and the mixture allowed to stand for three or four days. The excess of acid remaining is then titrated with one-fourth normal sodium hydrate, using as an indicator methyl-orange. The number of c.c. used is subtracted from 40; by then multiplying with 4.25, the number of milligrams of ammonia contained in 25 c.c. urine will be obtained. The urine should be perfectly fresh, and if concentrated or albuminous, at least five to eight days should be allowed to elapse before the acid is titrated.

CHAPTER VI.

QUALITATIVE AND QUANTITATIVE TESTS FOR ABNORMAL CONSTITUENTS.

Serum Albumin.—Before testing for albumin, all urines should be perfectly clear, as otherwise minute traces will be overlooked. Urines rendered turbid by bacterial growth frequently cannot be filtered directly, but must first be shaken with charcoal, Fuller's earth, burnt magnesia or talcum. All these substances may, however, carry down with them minute traces of albumin, so that it is desirable to examine every urine as fresh as possible. When the turbidity is due to urates, simple warming will suffice, since most albumin tests also react with water; but it may be desirable to also dilute the urine.

A peculiar and hitherto undescribed behavior of albuminous urines is mentioned by Hallauer. If normal urine is concentrated on the water-bath to half its volume and albumin then added, the boiling test will be strongly positive, but the ring and ferrocyanide tests absolutely negative. As soon as water is added a turbidity will appear. If the urine is still further concentrated to one-fourth its volume, even the boiling test will be negative. The substances which interfere with these reactions are, for the ring test, urea; for the boiling test, urea and neutral salts, and for the ferrocyanide reaction, the phosphates.

It is thus necessary to dilute concentrated urines before testing. This applies also to urines rich in urates, as many of the albumin tests will tend to throw these down. The reaction of the urine in every case should be acid. This may be effected by a few drops of acetic acid.

1. Heller's Ring Test.—A few c.c. of urine are layered over concentrated nitric acid, contained in a test-tube or a small, conical glass. In the presence of albumin, a sharply-defined white ring will appear at once, or after a few minutes, at the surface of contact. (Plate II.)

This test will reveal one part of albumin in 30,000 of urine, but is open to a number of objections: 1. In concentrated urines a crystalline ring of urea nitrate may form. This is prevented by diluting the urine. 2. If much uric acid is present, a ring of

PLATE II.

FIG. 2.

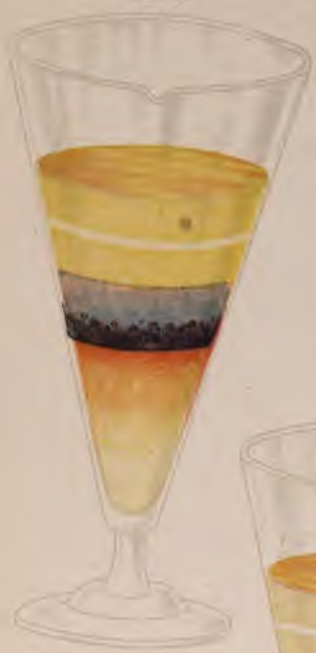


FIG. 4.

FIG. 1.

FIG. 3.

FIG. 5.

urates will form, but this is somewhat above the surface of contact and disappears on warming. 3. A rather diffuse ring, soluble in alcohol, occurs after the use of copaiba, tolu balsam and oil of santal. 4. Urines containing mucin and nucleo-albumins show a ring in about the middle of the layer of urine, which will dissolve on shaking the test-tube. 5. The nitric acid will oxidize the pigments, and will give rise to colored rings, which cannot, however, be mistaken for the albumin ring.

The ring test gives more information about the urine than any one test. Even in the presence of albumin, an excess of uric acid will show itself by the appearance of a distinct white ring above the zone of contact within five to ten minutes, while an absence of this ring will argue in favor of a diminished amount.

With more than 25 grammes of urea, an appearance like hoar-frost will be noted on the sides of the vessel, while with 45 or 50 grammes the nitrate will crystallize out. Urine containing bile will show a play of colors (of which the green is most characteristic), especially if the nitric acid contains traces of nitrous acid. Urobilin will give a ring of distinct mahogany color; indican a violet ring.

2. Boiling Test.—Five to 10 c.c. of urine are boiled, after which 5-10 drops of nitric acid are added. If a precipitate is formed on boiling, which does not dissolve upon the addition of acid, or if the precipitate only appears after the acid has been added, albumin is present. Sometimes urates precipitate out (avoid by diluting the urine), and occasionally resinous bodies will appear, but these dissolve readily on the addition of alcohol. If, after addition of nitric acid, the urine turns a distinct yellow and a white precipitate forms on cooling, the presence of albumoses is

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DESCRIPTION OF PLATE II.

THE NITRIC ACID TEST AS APPLIED TO THE URINE.

FIG. 1.—The light colorless ring in the clear urine above shows a slight increase in the amount of uric acid; the large white band denotes a large amount of albumin, bordering upon a colored ring, referable partly to indican (blue) and partly to urorosein.

FIG. 2.—The light ring in the clear urine above denotes a slight increase in the amount of uric acid. The bluish-black band is referable to an enormous increase in the amount of indican. (Ileus.)

FIG. 3.—The broad, light band in the clear urine above is referable to an enormous increase in the amount of uric acid. (Laparotomy.)

FIG. 4.—The color-play referable to the presence of bilirubin is shown in a diagrammatic manner.

FIG. 5.—The colored ring is referable to the presence of normal urinary coloring matter.

probable, since the urates, which might cause confusion, are generally of a dirty brown color.

A better way to perform the boiling test is to fill a test-tube two-thirds full of clear urine, and then to boil only the upper layers. A turbidity or precipitate which does not disappear, but becomes more distinct upon the careful addition of one or two drops of 2 per cent. acetic acid, is referable to albumin.

The urine may also be treated before boiling with a few drops of acetic acid until a distinctly acid reaction is obtained, and then with one-sixth its volume with saturated solution of magnesium sulphate or sodium chloride. Carried out in this manner, the test is absolutely certain.

3. Sulphosalicylic Acid (Salicylsulphonic Acid).—One of the simplest, most convenient and accurate of tests is performed by adding a pinch of sulphosalicylic acid to a few c.c. of clear urine in a test-tube. In the presence of albumin, a turbidity or white precipitate will form at the bottom of the tube. The test is especially recommended to the practitioner, as it necessitates only a small vial, with acid and a test-tube, and can thus be readily performed at the bedside. Alkaline urines should first be acidified slightly with dilute acetic acid, and warmed to drive off the gas. Albumoses and resins are also precipitated, but the former dissolve on warming and the latter upon the addition of alcohol.

Many books incorrectly state that urates are not precipitated, but in concentrated urines a granular deposit often forms on the sides of the tubes, or a white precipitate some distance above the layer of acid, which readily dissolves on heating. With minute traces of albumin, a turbidity is only apparent after several minutes. The test is one of the most delicate we possess; it will be positive with one part of albumin in about 60,000 of urine.

4. Ferrocyanide Test.—Five to 10 c.c. of urine are rendered strongly acid with acetic acid, after which 2-5 drops of a 10 per cent. solution of ferrocyanide of potash are added. In the presence of albumin, a turbidity or flocculent precipitate will form. In case a turbidity or precipitate is noticed before the addition of ferrocyanide, this is due to mucin or urates, and the urine should be filtered. An excess of ferrocyanide must be avoided, as it tends to dissolve albumin. Very concentrated urines may be negative pure, and positive when diluted, since the precipitate is somewhat soluble in solutions containing a high percentage of salts.

Albumoses and resins behave as in the previous test.

This test will detect albumin in a dilution of 1-50,000. It can

also be employed as a ring test by mixing a few c.c. of dilute acetic acid with several drops of ferrocyanide solution and carefully layering over the urine.

Potassium platinocyanide may be substituted for the ferrocyanide.

5. Spiegler's Test.—Spiegler's[1] reagent consists of corrosive sublimate, 8.0; tartaric acid, 4.0; glycerine, 20.0; distilled water, 200.0. Urine strongly acidified with acetic acid is allowed to float upon a few c.c. of this reagent, when a white ring will form. This test is one of the most delicate we possess, showing 1 part of albumin in 500,000 of urine; but if a small amount of salt only is present, it is less reliable. It also possesses the disadvantage that mucinous substance may be thrown down. In Jolles' modification 5 c.c. of urine are shaken with 1 c.c. of 30 per cent. acetic acid and 4 c.c. of a reagent consisting of sublimate, 10.0; succinic acid, 20.0; sodium chloride, 10.0; distilled water, 500.0. This is compared with another test-tube containing the same amount of urine, with 1 c.c. of acetic acid and 4 c.c. of water, since the acid will throw down the mucin. Urines containing iodine will throw down mercuric iodide, which is soluble in alcohol. Albumoses and nucleo-albumins are also precipitated.

Rössler has recently used Jolles' modification of Spiegler's test to determine if the albumin is of renal or other origin. He employs the test as a quantitative one by determining in how strong a dilution a ring will still form. Albumin due to nephritis will increase in amount after exercise or exertion, while albumin due to pus cells, etc., will remain the same.

6. Trichloracetic Acid.—By means of a pipette, 1-2 c.c. of an aqueous solution of trichloracetic acid of specific gravity 1.147 are carried to the bottom of a test-tube, containing the filtered urine. In the presence of albumin, a white ring will form at the zone of contact. Albumose and uric acid, if excessive, are also precipitated, but dissolve on heating.

7. Roberts' Test.—Roberts' solution is composed of one part of strong nitric acid and five parts of a saturated solution of magnesium sulphate. It is used in a manner similar to the nitric acid in Heller's ring test, and is subject to the same disadvantages, since it also throws down nucleo-albumin and mucin. The latter, moreover, is not dissolved as quickly as with pure nitric acid. It is less sensitive, and its only advantage is that it is not as corrosive nor as dangerous to handle.

[1] Deutsch. med. Woch, May 7, 1903.

Other Tests.—Carres places into a small test-tube 3-5 c.c. of a 25 per cent. aqueous solution of resorcin, and floats the urine to be examined over this with a pipette. In the presence of albumin, a white band will form at the zone of contact. A number of normal and abnormal urinary ingredients will also give rise to a white band, which is, however, said to dissolve on applying heat. The test is very sensitive, and reveals albumin where nitric acid has failed.

Riegler has discovered that beta-naphthol sulphonic acid possesses the property of precipitating all proteid substances. The reagent is prepared by dissolving 10 grammes of the crystals in 200 c.c. of distilled water, and then filtering. Five to 6 c.c. of the suspected urine are placed into a test-tube, and 20-30 drops of the reagent are then added. In the presence of albumin, turbidity or precipitation occurs at once. The reagent is very delicate, since 1 part of albumin in 40,000 of water will still give a distinct turbidity. The precipitate does not disappear on boiling, while albumoses, which are also thrown down, will redissolve when heated. By means of specially-constructed albuminometers, the reagent may also be used for the quantitative determination of albumin. Instead of beta-naphthol sulphonic acid, asaprol may be employed, but the urine must be acidulated first.

When no other reagents are at hand, alcohol will act as a fairly delicate test for albumin. It should be floated on the urine, when a white ring will appear at the surface of contact.

If a small crystal of metaphosphoric acid (HPO_3) be dropped into albuminous urine, the albumin will precipitate out as a white cloud. This test is not very delicate (1 : 1,000), and, like cold nitric acid, throws down a number of other substances. It possesses the advantage, however, of being solid when kept well stoppered.

Instead of metaphosphoric acid, picric acid may be used in substance or solution. It also precipitates albumose, peptone, mucin, nucleo-albumin, resins and urates.

Other tests of little practical importance are the phenol and tannic acid tests, and those with Tanret's reagent, phosphotungstic or phosphomolybdic acids. Many attempts have been made to introduce reagents in some convenient form for bedside use. Thus, Pavy recommends two tablets, consisting of citric acid and ferrocyanide of potassium, respectively, while Stütz-Furbringer's gelatine capsules contain bichloride of mercury, chloride of sodium and citric acid. A test-paper for the detection of albumin con-

sists of thick blotting-paper, which is impregnated (No. 1) with citric and (No. 2) with potasso-mercuric iodide. When testing for albumin, No. 1 is first added to the urine, and then No. 2. Though convenient, these methods should not be employed, since they lack in accuracy. Some of the methods described are so simple and require so little apparatus that there can be no excuse for resorting to test-paper, etc.

Summary.—It will be seen from the foregoing that none of the albumin tests are ideal, since they all throw down other substances closely allied to albumin, besides other foreign ingredients. Although albumoses, urates and resins can be easily distinguished from albumin, considerable difficulty often arises in distinguishing between nucleo-albumin and serum albumin. It is unfortunate that there is as yet no simple test for either of these substances, since it is often of the greatest importance to decide if the albumin is renal or nuclear in origin.

The following table will give an idea of the delicacy of the various tests:

Nitric acid (ring test)	1-30,000
Heat and acetic acid	1-50,000
Sulphosalicylic acid	1-60,000
Ferrocyanide test	1-50,000
Spiegler's test	1-500,000
Trichloracetic acid	1-75,000
Roberts' test	1-15,000
Resorcin test	1-50,000
Beta-naphthol sulphonic acid test	1-40,000
Metaphosphoric acid test	1-1,000

Quantitative Analysis of Albumin.—In many cases the intensity of the above reactions will give a fair idea of the amount of albumin present. Where greater accuracy is desired, the following may be employed, though none of them are ideal:

Esbach's Method.—Special graduated tubes are used, which are filled up to the mark U with urine, and the mark R with Esbach's reagent, consisting of picric acid, 10 grammes; citric acid, 20 grammes; distilled water, 1,000 c.c. The urine and reagent must be mixed very carefully by inverting the tube about a dozen times. At the end of twenty-four hours the precipitate will have settled to the bottom, and the amount can be read off in so many parts per thousand. The urine should be acid, and must be diluted if it contains more than 7 pro mill. albumin or is of a specific gravity higher than 1,010.

Since uric acid and other bodies will also precipitate, and the height of the precipitate will vary considerably with the tempera-

ture, the method is extremely crude. Recently attention has been directed to the fact that with some urines an abundant precipitate of picrate of kreatinin-potassium may form. This can, however, be recognized under the microscope by its crystalline structure.

Method of Brandenburg.—This method depends upon the fact that the lowest dilution of albumin urine which will give a ring with cold nitric acid is 0.033 ‰. Four dilutions of urine are prepared and tested separately: A = urine diluted 10 times; B = A + 2 parts of water; C = B + 4 parts of water, and D = C + 1 part of water. A ring in three minutes

with A = 0.33 ‰
" B = 1.0 ‰
" C = 5.0 ‰
" D = 10.0 ‰ } albumin.

Other dilutions can, of course, be made if necessary.

Method of Wassiliew.—Ten to 20 c.c. of urine are diluted up to 50 c.c. with distilled water, treated with two drops of a 1 per cent. aqueous solution of an aniline dye known as Echtgelb, and then titrated with a 12.5 per cent. solution of sulphosalicylic acid until a distinct brick-red color is obtained. The number of c.c. used multiplied by 0.00006 will indicate the amount of albumin in the 10 or 20 c.c. of urine examined. Vogel has recently tested this method, and has found it far from accurate.

The end reaction is by no means an easy one to determine, especially if the quantity of indicator recommended by Wassiliew, two drops, is employed. It was found that the use of 10-12 drops produced a much sharper end reaction, without any apparent decrease of sensitiveness. The most advantageous technic found by Vogel is as follows: If necessary, the urine is acidified with acetic acid, and 10 c.c. each are measured out into several evaporating dishes. After the addition of the indicator, the reagent is run in very slowly from a burette, with constant stirring, as the union of acid and albumin is somewhat slow. The first portion tested is taken as control, and after the end reaction is reached, as denoted by the production of a red color, which is not deepened by the addition of a further drop, a slight excess is run in. Titration is then carried out in the other dishes until the same shade of color is obtained.

In order to control the results, a number of gravimetric estimations were made. Where the amount of albumin was above 0.15 to 0.2 per cent., fairly constant figures were obtained, but with

less the error was so high that the sulphosalicylic acid method can lay no claim whatever to accuracy. Even normal urine requires a certain amount of sulphosalicylic acid before the end reaction is obtained, but this is not a constant factor.

By Boiling.—This method, though troublesome, is at present the only accurate one we possess. A small sample of urine is boiled in a test-tube, filtered and the filtrate tested with ferrocyanide of potash and acetic acid for albumin. If negative, the entire quantity (500-1,000 c.c.) should be boiled; but if positive, 50 per cent. acetic acid should be added, drop by drop, until boiling will completely precipitate all albumin present. The urine is then poured on a dried filter of known weight, care being taken that none of the albumin will remain behind in the flask. The precipitate should then be washed until the filtrate no longer turns turbid with silver nitrate and nitric acid. Fats are removed by alcohol and ether; finally the filter and its contents are dried at 120-130° C. until a constant weight is obtained. If still greater accuracy is desired, the precipitate is incinerated so that the amount of mineral ash present may be deducted from the weight found.

Other Methods.—The differential density method consists in taking the specific gravity of urine before and after the removal of albumin by heat and acetic acid. The decrease in the specific gravity multiplied by 400 will indicate the number of grammes of albumin in 100 c.c. of urine.

Esbach's method has been modified by centrifuging the precipitates in special graduated tubes, instead of waiting twenty-four hours until the precipitate has settled. Very recently two new methods have been suggested, one depending on the change of the index for refraction if albumin is present, and the other on the ultramicroscopic examination of a drop of urine. Since, however, they necessitate very expensive apparatus, they will hardly come into general use.

Serum Globulin.—It is generally assumed that serum globulin occurs in two forms, viz., euglobulin and pseudoglobulin. These are detected as follows: The phosphates are filtered off after precipitation with ammonium hydrate. The filtrate is then treated with an equal volume of saturated ammonium sulphate, when any precipitates will be referable to serum-globulin. For quantitative estimation, the precipitate is collected, washed with half-saturated ammonium sulphate, dried and weighed.

Albumoses.—Albumin must first be removed by boiling with an equal amount of 10 per cent. trichloracetic acid and filtering

while hot. Ordinary acetic acid will not do, since this would change some albumin to albumose. Fifty c.c. of urine are acidified in a beaker with 5 c.c. of hydrochloric acid, precipitated with 2-3 c.c. of 10 per cent. phosphotungstic acid, and heated over a free flame. In a short time the precipitate will collect at the bottom of the beaker in the form of a resinous mass. The supernatant fluid is now poured off, and the precipitate washed twice in distilled water. The precipitate is then covered with about 8 c.c. of distilled water and treated with 0.5 c.c. of a sodium hydrate solution of a specific gravity of 1.16. The solution will assume a dark-blue color, and is heated until it turns a grayish-yellow. A small portion is then poured into a test-tube, allowed to cool and a few drops of dilute copper sulphate solution added. In the presence of albumose, the solution will now turn red (biuret test). If urobilin is present, a positive reaction may be obtained in the absence of peptone, hence the urine should first be treated with lead acetate, or only small quantities, such as 10 c.c., of urine employed.

A simple way of detecting albumoses is to acidify the urine strongly with acetic acid, and then to add an equal volume of saturated solution of common salt. If albumoses are present, a precipitate occurs, which dissolves on boiling and reappears on cooling. In the presence of serum-albumin, the boiling fluid should be filtered.

Albumose may still further be demonstrated by adding sodium hydrate and very dilute copper sulphate to the filtrate, when a pink color will appear (biuret reaction), or by boiling it with Millon's reagent (red color).

A very satisfactory test, which does not react with moderate amount of urobilin, is that of Bang.[1] Ten c.c. of the suspected urine are boiled with 8 grammes of powdered ammonium sulphate. The fluid is then centrifuged, the supernatant fluid poured off and the sediment stirred with alcohol in an agate mortar. After the alcohol is poured off, the sediment is boiled with a little water and treated with sodium hydrate and copper sulphate, as before.

Peptone.—Three hundred c.c. of urine are saturated with ammonium sulphate at 60-70° C., filtered on cooling, rendered alkaline with sodium carbonate, again saturated between 60° and 70° C., filtered, neutralized with dilute acetic acid and saturated a third time between 40° and 50° C., cooled and filtered. The filtrate is diluted with an equal amount of distilled water, and

[1] Deutsch. med. Woch., 1898, p. 17.

treated, drop by drop, with a fresh solution of tannic acid. The precipitate is filtered off the following day, dried, powdered and covered with a small amount of baryta water, containing an excess of baryta. After heating on a water-bath for two or three minutes, the mixture is set aside one to two hours, and then filtered. A positive biuret test will finally indicate the presence of true peptone.

Bence Jones Bodies.—A urine containing Bence Jones albumose will show the following reactions: 1. If the filtered urine be heated up to 55°-60° C., a turbidity will form, which disappears at 80°-85° C., but reappears as a flocculent precipitate on cooling. 2. With Heller's ring test, a white ring will form at the line of junction of urine and acid. On heating, this disappears, but also reappears as a flocculent precipitate on cooling. 3. A more or less distinct biuret reaction can be obtained. 4. The addition of 33 per cent. acetic acid at ordinary temperature causes no turbidity, not even if considerable acid is employed and the urine boiled. 5. On standing for some time, fatty crystals, the so-called spheroids of Naunyn, will separate out. The proteid is furthermore precipitated by sodium chloride in an acid urine before complete saturation, and will give the xantho proteic and other color reactions for albumin as a class. For a number of other reactions, of interest only to the physiological chemist, the reader is referred to the article by Jochmann and Schumm.[1]

Nucleo-albumin.—The test for nucleo-albumin given in most works is the following: A test-tube two-thirds full of urine is treated with about 10-20 drops of a 50 per cent. solution of acetic acid and set aside. After a few minutes the test-tube is compared with another one containing urine not treated with acid, when a distinct opalescence will be observed. It has been shown, however, that this is not due to nucleo-albumin, but to a fibrinogen and euglobulin. With the exception of the crude nitric acid test, there is as yet no simple method of detecting nucleo-albumin. The complicated tests necessary depend upon the presence of phosphorus in the molecule.

A considerable quantity of urine—about 100 c.c.—is acidulated with acetic acid, and the precipitate filtered off, washed in water and rubbed up in a mortar with a little sodium carbonate solution. If the precipitate does not dissolve entirely, it may be necessary to add a little sodium hydrate. The phosphates are removed by filtering, re-precipitating and washing with water. The final

[1] Zeitsch. f. klin. Med., vol. 46, p. 445.

precipitate is divided into two portions. One is shaken up with 25 c.c. of 33 per cent. hydrochloric acid, the mixture boiled gently for ten minutes, allowed to cool, rendered alkaline with sodium hydrate and a few drops of copper sulphate (dilute) added. After boiling, cooling and allowing to settle, mucin, if present, will give rise to a red deposit of copper oxide. The other portion is rubbed up with a little alcohol and boiled on a water-bath. The precipitate is filtered off, washed with alcohol, shaken up with ether, allowed to stand for a while, filtered, dried and then fused with thirty parts of a mixture of sodium carbonate one part, potassium nitrate three parts. The fused mass is dissolved in nitric acid and boiled, then about 5 c.c. of a solution of ammonium molybdate (10 per cent.) are added. A yellow precipitate indicates the presence of phosphorus, which could only come from nucleo-albumin.

Fibrin.—The clots of suspected fibrin should be collected, washed and dissolved in a 1 per cent. solution of soda or a 5 per cent. solution of hydrochloric acid. On cooling, the solution is tested as for serum albumin.

Histon.—Albumin, if present, is removed. The urine is then precipitated with alcohol, and the precipitate dissolved in boiling water. On cooling, hydrochloric acid is added, and the urine allowed to stand several hours, when any cloudiness is filtered off and the filtrate precipitated with ammonia. The precipitate is washed with dilute ammonia and dissolved in dilute acetic acid. If the biuret test is positive and coagulation occurs on heating, histon is present.

Quantitative Test of Globulin, etc.—While the use of Esbach's albuminometer will give a rough idea of the amount of albumin present in urine, it will not tell what kind of albumin is being dealt with. Oswald[1] has very recently modified the test in the following way: Four albuminometers are taken, and each filled up to the mark U with urine from a burette, the amount of urine necessary being noted. Tube A is filled in the usual manner up to R with Esbach's reagent, and the total amount of albumin determined. In the other tubes the different forms of albumin are precipitated with various amounts of concentrated solution of ammonium sulphate. Thus tube B received 2.8 c.c. to 7.2 c.c. of urine, corresponding to a saturation of 28 per cent.; tube C, 3.6 c.c. to 6.4 c.c., corresponding to a saturation of 36 per cent., and tube D, 5 c.c. to 5 c.c., corresponding to a saturation of

[1] Münch. med. Woch, Aug. 23, 1904.

50 per cent. Each albuminometer may be marked with a glass pencil, so that accurate measurement is not necessary in subsequent cases. After twenty-four hours each precipitate (except that in tube A) is collected on a small filter, dissolved in water with the addition of a little sodium carbonate, diluted up to the mark U in an albuminometer, and then re-precipitated with Esbach's solution up to the mark R. The following results will be obtained:

Albuminometer B will contain fibrinogen and fibrinoglobulin.
Precipitate albuminometer C minus that of B = euglobulin.
Precipitate albuminometer D minus that of C = pseudoglobulin.
Precipitate albuminometer A minus that of D = total albumin.

The following are the results of a number of cases examined by the author of this method:

	A Total Albumin ‰	B Fibrinogen ‰	C-B Euglobulin ‰	D-C Pseudo-globulin ‰	A-D Serum Albumin ‰
Acute scarlatinal nephritis	10	0	2.5	1.5	6
Acute advanced nephritis	12	0	0	0.5	11.5
Acute nephritis	5	0	0.25	1.25	3.5
Chronic nephritis (1)	4	0	trace	1	3
Chronic nephritis (2)	8	0	trace	2	6

Where only traces are present, it may be advisable to use specially-constructed Esbach tubes, with very narrow bottom.

Sugar.—Since the evening sample often contains sugar and the morning sample not, both should be examined; and in quantitative work, a sample of the entire amount of twenty-four hours. Since moderate degrees of glycosuria disappear with strict diet, the patient should be instructed to take some carbohydrate on the day before.

Life insurance examiners have been frequently misled by patients who have been previously instructed by their family physician to carefully avoid starch and sugar for a certain time before presenting themselves for examination. The urine must be sent as fresh as possible, as it often contains yeast, which tends to decompose traces of sugar. In every case albumin should first be removed by boiling and filtering, unless present in mere trace.

But few of the sugar tests are absolutely conclusive in the positive sense, and cases are wrongly pronounced diabetic every day because the careless examiner has failed to confirm a doubtful reaction with one or more other tests. There is only one specific reaction for sugar, and that is its property to ferment in the presence of yeast.

1. *Nylander's Test.*—The simplest, most convenient, and at the same time one of the most accurate, tests for detecting the

presence of glucose in urine is by means of Nylander's reagent (Rochelle salts 4 grammes, bismuth subnitrate 2 grammes, and sodium hydrate 10 grammes, are dissolved in 90 c.c. of water, heated to the boiling point and filtered on cooling. Should be kept in a dark bottle). To a few cubic centimeters of urine in a test-tube about one-tenth of the amount of reagent is added, and the mixture then boiled briskly over the Bunsen flame. In the presence of sugar the mixture will turn black at once, or soon after boiling, owing to the reduction of the dissolved bismuth to sub-oxide of bismuth. With mere traces of glucose, the fluid will merely turn brown, but will appear black with transmitted light. Reduction after cooling is of no significance. Urines free from sugar are not altered, or else will throw down a white precipitate, consisting of phosphates.

The test is absolutely conclusive only in a negative sense, since there are many substances other than sugar which will cause partial or complete reduction (pigmentary bodies, chiefly uroerythrin, hematoporphyrin, indoxyl-glycuronic acid, ammonium carbonate, hydrogen sulphide, mucin and albumin). In the presence of 0.6 per cent. albumin a red precipitate will be produced, while 1-2 per cent. causes a black sediment, not unlike that due to sugar.

A number of drugs will also cause ready reduction. Among these are rhubarb, senna, kairin, tincture of eucalyptus, oil of turpentine, quinine, antipyrine, acetanilid, arsenic, salicylic acid compounds, sulphur, mercurials, santonin, tannic acid, chloralhydrate, benzol, sulphonal, trional, sodium benzoate, large doses of creosote and podophyllo-toxin.

These foreign bodies can, however, be removed to some extent by first precipitating the urine with acetate of lead, or by acidifying with acetic acid, boiling and filtering, in case of albumin. In doubtful cases the polariscope or fermentation test should always be used as control. Care should be exercised in boiling urines containing an excess of mucin, since the alkali in the reagent renders this stringy, and the mixture is liable to splutter.

Recently a stronger Nylander's solution has been recommended (containing about 8 per cent. bismuth). It works more rapidly, but is more apt to react with bodies other than glucose.

2. *Brücke's Test.*—Brücke uses the following reagent: 1.5 grammes of freshly-precipitated bismuth subnitrate are heated to boiling with 20 c.c. distilled water; 7 grammes of potassium iodide are then dissolved in the mixture, which will turn red. Finally, 1.5 grammes of hydrochloric acid are added. Two test-tubes are

filled to the same height, one with water and the other with the urine to be examined. Sufficient hydrochloric acid is added to the water, so that a drop of the reagent no longer causes a precipitate, and the same amount of acid is then added to the urine. This is followed by the reagent until precipitation is complete, after which the whole is filtered. The filtrate should show no turbidity upon adding reagent or acid. An excess of potassium or sodium hydrate is then added, and the mixture treated as in Nylander's test.

This test is rarely employed. It also reacts with the glycuronic acid compounds and with pigments, but the presence of albumin is not a disturbing factor.

3. *Maschke's Test.*—The albumin is here removed by adding three or four times the amount of a solution consisting of sodium tungstate 30 parts, 30 per cent. acetic acid 75 parts, distilled water 120 parts. The urine is then filtered and treated with a few drops of reagent. If no precipitation occurs, half the volume of concentrated sodium hydrate and a pinch of bismuth subnitrate are added, and the mixture heated. A black precipitate will indicate sugar, but if only a brownish discoloration appears, or a black precipitate on prolonged boiling, only physiological traces are present.

Sources of error are pigments, glycuronic acid and hydrogen sulphide.

4. *Fehling's Solution.*—This consists of equal parts of a copper and an alkaline solution. The copper solution consists of copper sulphate 34.639 grammes in 500 c.c. of water (approximately 1 ounce to the pint); the alkaline solution of 173 grammes Rochelle salts and 125 grammes of potassium hydrate in 500 c.c. of water (approximately 6 ounces and 4 ounces to 1 pint). These should be mixed fresh and boiled, after which a small amount of urine is added, and the mixture then heated short of boiling. In the presence of sugar, the fluid will first become opaque, then yellow and red, and after standing a red precipitate is thrown down. Mere turbidity, with green or yellowish discoloration, is of no significance.

This test is open to the same objections as Nylander's, since a number of foreign substances may occur in the urine, which give a partial reduction and leave one in doubt as to whether traces of glucose are present.

It is generally stated that there are two classes of bodies which interfere with the reaction: those which, in addition to glucose, cause copper reduction, and those which will prevent the reduction.

The former include the urates and purin bases, kreatinin,

indican, alkapton, hippuric acid, nucleo-albumin, urinary pigments, glycuronic acid, pyrocatechin, hydrochinon, other sugars, alkaloids, arsenic, tannic and gallic acid, pyrogallol, camphor, copaiba, cubebs, chrysophanic acid, salicylates, oxalic acid, chloral, turpentine, glycerine, sulphonal, thallin, benzoic and carbolic acid. The reduction caused by these substances is never, however, as complete as with glucose; that is, precipitation occurs only on boiling or when cooled off, and by mere heating short of boiling only a discoloration occurs.

Substances which retard the reaction, even if glucose is present, are albumin and some of its products, salts of ammonia and saccharin.

5. *Trommer's Test.*—This depends also upon the reduction of copper sulphate to cuprous oxide.

A few c.c. of urine are rendered alkaline by one-third the amount of 10 per cent. potash or soda lye, and then treated, drop by drop, with a 10 per cent. solution of copper sulphate, until the cupric oxide formed is no longer dissolved. On boiling, a yellowish precipitate of cuprous hydroxide is formed, which will gradually settle as the red cuprous oxide.

This test is open to the same objections as Fehling's. It is also more reliable if the heating is interrupted short of boiling, but then faint traces of glucose often escape detection.

Fehling's and Trommer's tests have been modified in a number of ways to avoid error. Dilution of the urine is a very valuable procedure, unless mere traces of glucose are present, when these, too, will escape detection. Johnson removes all the reducing substances by adding to the urine one-twentieth its volume of saturated sodium acetate and one-fortieth its volume of saturated corrosive sublimate. After forty-eight hours the precipitate is filtered off. The excess-of mercury is then removed by hydrogen sulphide, and the latter removed by boiling.

Repeated filtration through animal charcoal will also remove a large percentage of reducing substances. It was formerly believed that some glucose is also filtered out by this procedure, but Rudisch has shown that this amount is so slight as not to interfere with the quantitative estimation. The charcoal should be animal, and free from impurities. After repeated filtration, the urine will flow through almost colorless, yet occasionally may reduce copper, even where sugar is absent.

Worm-Müller's modification depends on the fact that at a temperature below 70° C. reducing substances other than glucose react only to a slight degree, or not at all.

The reagent is prepared by dissolving 10 grammes of Rochelle salts in a 4 per cent. solution of sodium hydrate; 2.5 c.c. of this solution are heated with 1 c.c. of a 2.5 per cent. solution of copper sulphate just short of boiling. Five c.c. of the urine to be examined, freed of albumin, are heated to the same degree at the same time. Ten to twenty-five seconds are allowed to escape, after which the urine is added in small portions to the reagent. If glucose is present, red cuprous oxide will soon separate out. If the reaction does not occur, the test should be repeated, with increased amounts of copper sulphate solution, until 4.5 c.c. are utilized for one test.

Among other modifications, Haines' and Elliott's possess the advantage that only very small amounts (8 drops) of urine are necessary. Haines uses a reagent consisting of copper sulphate 2 grammes, glycerine 15 grammes, liquor potassæ 150 c.c., water to make 200 c.c. Half a test-tube of the solution is heated to boiling first alone, and then with 6-8 drops of urine.

Pavy's method is similar to Rudisch's for quantitative work. Owing to the presence of ammonia, the precipitate remains dissolved, and the blue solution simply becomes colorless. It is open to the same objections as the other methods.

6. *Moore's Test.*—If urine containing glucose is boiled with one-third its amount of 10 per cent. potash or soda lye, it will turn dark brown or intensely brownish-yellow. Dilute urine will give a pure yellow color.

This test is fairly delicate, but has been replaced by those already mentioned, since less reliable. It also reacts with mucin, proteids, biliary pigments and alkapton. These may be removed to some extent by boiling and filtering through charcoal.

7. *Rubner's Test.*—Ten c.c. of urine are treated with an equal amount of saturated solution of acetate of lead and filtered. Ammonia is then added, drop by drop, to the filtrate, until the precipitate no longer dissolves. On heating up to 88° C. in the water-bath, the precipitate will turn pink. This test is too complicated for routine work, though delicate and reliable.

Stern thinks very highly of it, and states that, when properly performed, only certain glycuronic acid compounds may give rise to error. He has modified the test as follows: Take from 1-5 c.c. of urine and add to it an equal amount of ammonia hydrate, then add about 5 drops of strong solution of lead acetate. A white, flocculent precipitate, composed of sulphate, phosphate and chloride of lead and hydrated lead oxide, will appear immediately.

Heat gently a part of the sediment over an alcohol lamp until two or three bubbles rise to the surface. If glucose is present, there will appear in the heated region of the sediment a well-defined, pink spot, the intensity of which is dependent on the amount of glucose present. With less than 0.1 per cent. glucose, the spot will appear yellowish. It is best to conduct the test in test-tubes of the smallest calibre, which have been previously well cleaned. Urines of a specific gravity higher than 1,010 should be diluted before the test is applied.

8. *Heating Test.*—Where no reagents are at hand, a small quantity of suspicious urine may be evaporated to dryness in a porcelain or other available dish. If the heating is continued, the residue will become brown and sticky in the presence of sugar, and an odor of caramel will be emitted.

9. *Methylene Blue Test.*—Frölich recommends the following procedure: Ten c.c. of urine are treated with 5 c.c. of concentrated solution of neutral lead acetate and the same amount of concentrated solution of basic lead acetate, and filtered through a dry filter. Some of the filtrate is placed into a test-tube; into another an equal amount of 1-300 aqueous solution of methylene blue. The latter is rendered alkaline with one-fifth its amount of 10 per cent. solution of potassium hydrate and warmed. Now the filtered urine is added, and the fluid heated to boiling. In the presence of dextrose the bluish-black mixture will turn lighter, and finally become yellowish and transparent. The decolorization occurs almost always within twenty or twenty-five seconds after boiling. The decolorized fluid will again turn bluish on shaking, but this will disappear on standing.

The great drawback of the method lies in the fact that every normal urine will possess reducing properties corresponding to 0.1 per cent. glucose. Levulose and kreatinin may also interfere.

10. *Picric Acid Test.*—If saccharine urine is heated with an equal bulk of saturated solution of picric acid and some potassium or sodium lye, a dark cherry coloration will result, owing to the formation of picramic acid. The source of error is, however, great, since even normal urine will show the reaction to a slight extent, owing to the presence of glycuronic acid. Other substances which interfere are uric acid, kreatin, kreatinin, acetone and pigments.

11. *Sodium Sulpho-indigotate Test.*—If a solution of indigotin-disulphonic acid is saturated with sodium carbonate and boiled with a solution containing sugar, it will turn green, purple, red and

yellow. On shaking the still warm solution, it will again change color in the reverse order. A number of other substances also give the reaction, especially glycuronic acid, inosite, lactose, gallic, tannic and salicylic acid and their compounds.

12. *Hoppe-Seyler's Test.*—To 5 c.c. of a 0.5 per cent. solution of orthonitro phenylpropiolic acid in caustic soda and water, 10 drops of the urine to be tested are added, and the mixture then boiled half a minute. If the solution turns dark blue, at least 0.5 per cent. sugar is present. Though not very delicate, the test seems to be fairly reliable, since only lactose and indoxyl cause the same reaction.

13. *Penzoldt's Test.*—If to urine rendered alkaline, paradiazobenzolsulphonic acid is added, a red coloration, turning to violet in ten to fifteen minutes, will be observed. In proper dilution, the mixture will show an absorption band between D and F, and another one at G. The reagent is difficult to handle, since explosive, and also reacts with albumin, acetone, phenol and pyrocatechin.

14. *Furfurol Test.*—If 1 c.c. of concentrated sulphuric acid is allowed to run beneath 0.5 c.c. of a dilute sugar solution, containing one drop of a 15 per cent. alpha naphthol solution, a green ring will form at the surface of contact, which is soon followed by a dark violet ring above this. If the mixture be shaken, it will turn cherry red, with a bluish hue. With the spectroscope a narrow band may be detected between D and E, to be followed by a band beginning at F and extending to the violet end. The reaction is due to the formation of furfurol by the action of sulphuric acid on sugar. Instead of alpha naphthol, thymol or xylidin may be used. The latter may be employed in the form of test-paper, as follows: Strips of paper are saturated in a mixture composed of equal volumes of xylidin and glacial acetic acid, to which some alcohol has been added. If the dried paper is held over saccharine urine heated with sulphuric acid, furfurol will be given off and will color it red. Other substances which react like sugar are other sugars, glucosides, albumin and peptone.

15. *Horsley-Pratesi's Test.*—2.5 grammes potassium hydrate are dissolved in 60 grammes of a very strong solution of potassium silicate (water glass), to which 2 grammes of potassium bichromate are added. A drop of the reagent is then placed on a small strip of tin and dried by holding over the flame. Four drops of the reagent are evaporated on the same spot. A drop of the suspected urine is then allowed to come in contact with the evaporated

reagent and heated. A green color will appear in the presence of sugar, but albumin, glycuronic acid and pigments will give the same reaction.

16. *Fermentation Test.*—Any fluid containing glucose will readily ferment in the presence of yeast. Since the glucose will split up into alcohol and carbon-dioxide, its presence will manifest itself by the formation of gas. The cheapest and most suitable apparatus is the Einhorn fermentation tube, but certain precautions are necessary in its use. The urine should not be shaken with the yeast, since a certain amount of air will be entangled,

FIG. 25.

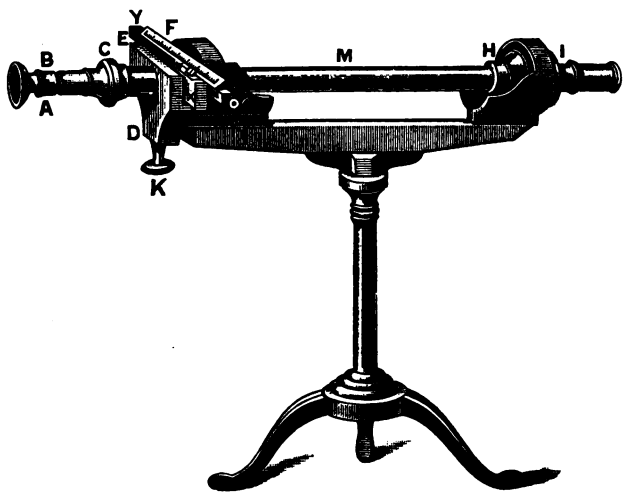
Einhorn's saccharimeter.

which will slowly rise after the mixture is poured into the tube. It is best to let the urine stand a few minutes after the yeast has been added, and then to distribute the latter gently with a glass rod before pouring into the tube. In addition, the tube may be inclined on a suitable clamp before setting aside. Fermentation is more active in a warm place, so that the tube is best placed in the incubator or near a stove during cold weather. At the end of twelve hours fermentation will be nearly complete, and a small or large volume of gas in the long arm will establish the presence of glucose in all doubtful cases. When there is some doubt as to the nature of the gas, the tube may be inverted under water, so that the

gas can escape into a test-tube filled with lime-water, which will not be affected by air, but will turn turbid in case of carbon-dioxide. Since some yeast is self-fermenting, it is often advisable to make a control test with urine free from sugar or with water. When the Einhorn fermentation tubes cannot be procured, the mixture of urine and yeast may be poured into a test-tube, which is then inverted into a vessel containing mercury.

The fermentation test is the only absolutely certain test for sugar, since nothing but sugar will react with yeast. There may, however, be some doubt as to the kind of sugar, since maltose and other carbohydrates will also yield carbon-dioxide. These, how-

FIG. 26.



Soleil-Ventzke's saccharimeter.

ever, occur so rarely that they may be practically disregarded. Occasionally a urine containing appreciable amounts of sugar will not ferment, since some preservative has been added or since the patient has taken antifermentative drugs, which have passed into the urine.

17. *Polariscope.*—The simplest way of detecting the presence of sugar in urine is by means of the polariscope. Since albumin is levuloratatory, it must first be removed by acidifying slightly with acetic acid, boiling and filtering. If the urine is not absolutely clear, and if too highly colored, lead acetate in substance or solution should be added, as the resulting precipitate will carry down the suspended matter and the pigments. The resulting pale

fluid is filled into the glass tube, then placed in the instrument. The readings are best taken in a dark room, with sodium or strong electrical light.

Certain precautions are necessary. Thus, the tube must be absolutely clean and dry, and in filling, bubbles of air should be avoided. Every normal urine turns the plane of polarized light to the left (0.1 — 0.3 per cent.), hence for the detection of traces of sugar two polarimetric readings are necessary, one before fermentation and another after. Diabetic urine frequently contains β-oxybutyric acid, which also turns to the left; its presence is rendered probable by the detection of acetone and diacetic acid. Here, also, two readings are necessary.

Conducted with a delicate instrument, polariscopy is a very reliable means of detecting sugar in urine. It must be remembered, however, that dextrorotation, unlike fermentation, is not specific for glucose. Glycuronic acid may be present, or the ingestion of certain drugs (morphine, etc.) may also cause a rotation to the right. Then, also, the presence of levulorotatory substances, such as albumin, levulose, β-oxybutyric acid, cystin and certain drugs, may neutralize the dextrorotation and lead one to believe that no sugar is present.

18. *Phenylhydrazine Test.*—Five c.c. of urine are treated with 0.5 gramme phenylhydrazine hydrochlorate and twice the amount of sodium acetate. The test-tube containing the mixture is placed in a water-bath and heated for half an hour, then chilled by immersing in a beaker with cold water. Characteristic, needle-shaped crystals will adhere to the sides and bottom of the test-tube, and can be readily identified by microscopical examination. (Plate III.)

Riegler[1] has modified the phenylhydrazine test as follows: One c.c. of urine is treated with a pinch of phenylhydrazine oxalate and 10 c.c. of water. After boiling, 10 c.c. of a 10 per cent. solution of caustic potash are added, and the test-tube shaken thoroughly, when a beautiful reddish-violet color will appear within one minute in the presence of at least 0.05 per cent. glucose. Havelburg recommends that 1.2 grammes phenylhydrazine hydrochlorate and 1.8 grammes sodium acetate be warmed with 10 c.c. of distilled water. Ten c.c. of the suspected urine are then added, with 8-15 drops of chloroform. The chloroform will soon fall to the bottom, and if sugar is present a fluid layer will be found above it, in which the characteristic crystals are contained.

[1] Deutsch. med. Woch., April 9, 1904.

PLATE III.

Phenylglucosazon Crystals obtained from a Diabetic Urine. (Simon.)

Substances besides glucose which form crystals of osazone are levulose, maltose and pentose. These can only be distinguished by their different melting point, solubility and optical behavior.

Summary.—A rather full list of sugar tests has been given, since almost all are open to some objection and have some defect, so that there may be occasion to employ several to confirm a diagnosis of diabetes. Those most commonly employed are Nylander's, Fehling's and the fermentation test. The most reliable are Rubner's, the fermentation and polariscope test, while the others are only rarely resorted to.

The following table gives an idea of the delicacy of the various tests:

	Per Cent
Nylander's test	0.1
Brücke's test	0.2
Maschke's test	0.2
Fehling's test	0.3
Trommer's test	0.1
Filtration through charcoal	0.01
Worm—Müller's test	0.25
Haine's test	0.2
Elliott's test	0.2
Pavy's test	0.2
Phenylhydrazine test	0.03
Moore's test	0.5
Rubner's test	0.1
Methylene blue test	0.4
Picric acid test	0.1
Sodium-sulphoindigotin test	0.1
Hoppe-Seyler's test	0.5
Penzoldt's test	0.1
Furfurol test	0.02
Horsley-Pratesi's test	0.4
Fermentation test	0.1
Polarization	0.1

It occasionally happens that in rare cases it is necessary to separate the glucose from the urine. This is done as follows: A large amount of urine is evaporated to a thin syrup, then about half the amount of ether is added. The mixture is then allowed to evaporate, when, after several days, the syrup will have crystallized. The urea and extractive matter are removed by treating the crystals with a small amount of alcohol. The residue is then dissolved in boiling alcohol, the solution filtered while hot, and the filtrate allowed to crystallize. The separated crystals are repeatedly subjected to crystallization from methyl alcohol. They form four-sided prisms, which melt at 141-146° C. and dissolve slowly in water, alcohol and methyl alcohol; more readily in boiling alcohol, but not at all in ether. With large amounts of urine, traces of these crystals may be found even in normal urines.

Quantitative Estimation of Sugar.—1. *Fehling's Method.*—Since 10 c.c. of mixed Fehling's solution corresponds to 0.05 glucose, an accurate quantitative analysis is possible. Ten c.c. of the Fehling's solution are diluted with 40 c.c. of water and boiled. The urine is diluted five (if specific gravity is below 1,030) or ten (if specific gravity is above 1,030) times, poured into a burette and added in small quantities to the boiling Fehling solution until all of this has precipitated as red cuprous oxide and the supernatant liquid is colorless. The degree of dilution multiplied by 5 and the result divided by the number of c.c. of diluted urine employed will give the percentage of sugar. Owing to the fact that it is difficult to determine the end reaction, a small portion of the Fehling's solution may be filtered, and then treated with acetic acid and ferrocyanide solution. If unreduced copper is still present, a brown color is obtained. More accurate results are generally obtained with the modification of Rudisch,[1] who uses the following solution: Copper sulphate, 4.78 grammes; sodium sulphite, 50 grammes; crystallized sodium carbonate, 80 grammes; 10 per cent. water of ammonia to make 500 c.c.. One c.c. will correspond to 0.001 glucose. The urine is first decolorized with charcoal, then 10-20 c.c. of the standard solution are placed into an Erlenmayer flask and diluted with 50 c.c. of water. When boiling, the urine is allowed to flow in from a burette until the solution is decolorized. Approximate titration may be done with a Beck's burette.

Citron[2] heats to boiling 1 c.c. of urine with 20 c.c. of Fehling's solution in a dish with some water. The sediment is then filtered through paper with the aid of some powdered pumice stone, and washed with hot water. The filtrate is acidified with sulphuric acid until decolorized, and finally 1 gramme of potassium iodide and some starch solution added. On now titrating with decinormal thiosulphate of sodium, a point will be reached where the blue-black color turns white. A specially-constructed burette is used, which will indicate the percentage of sugar.

Owing to the fact that the usual estimation by means of Fehling's solution is often difficult and inaccurate, Harvey G. Beck[3] has quite recently recommended the following modification: A beaker is filled one-third with water and placed over the Bunsen burner. Four centrifugal tubes, graduated at 2 c.c., are filled accurately to the mark with standard Fehling's solution, numbered 1, 2, 3 and 4, respectively, and transferred to the beaker. As soon

[1] Jacobi Festschrift.
[2] Münch med. Woch., Nov. 24. 1903.
[3] Medical News, Sept. 3, 1904.

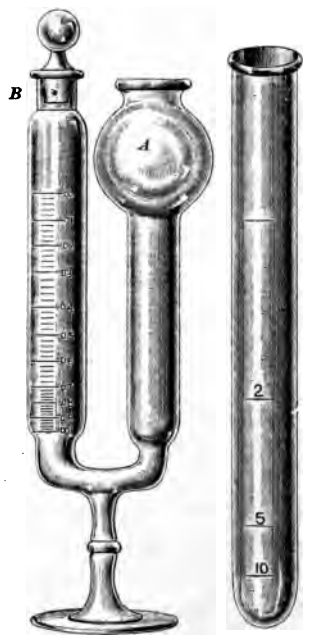
as the water boils, the tubes are removed and placed into a tube holder in their proper order. By means of a pipette, graduated into twentieth c.c., four-twentieth c.c. of the urine to be examined is allowed to flow into tube No. 1, the other tubes each receiving one-twentieth more. Thus, four-twentieths are added to No. 1, five-twentieths to No. 2, six-twentieths to No. 3 and seven-twentieths to No. 4. The tubes are violently shaken, so as to mix thoroughly the urine and reagent, after which they are returned to the beaker and allowed to remain in the boiling water for three minutes. Red cupric oxide will be precipitated, and the color of the supernatant fluid can be readily determined by allowing the sediment to settle, or, better still, by placing the tubes in the centrifuge. If the fluid above the sediment is still blue in tube No. 4, four-twentieths c.c. more are added to each of the tubes, increasing the amount of urine respectively to eight, nine, ten and eleven-twentieths. These steps are repeated until complete decolorization is obtained, when the first tube in the series completely decolorized is chosen. Twenty divided by the number of twentieth c.c.'s used will then give the percentage of sugar present. To determine the end reaction more definitely, one-twentieth c.c. may be added to each tube after sedimentation in such a manner as to form a thin layer on the surface, after which the tubes are returned to the beaker without agitation, when a yellow ring of cuprous oxide will form in those tubes where reduction is incomplete. The advantages claimed by the author are: (1) With a little practice the estimation can be completed in less than ten minutes. (2) With reasonable care, the results are much more accurate. (3) By means of the number of tubes, several can be used for control tests, thus one can make two or more determinations at the same time. (4) The solution never reaches the boiling-point, and such bodies as uric acid, kreatin, kreatinin, nucleo-albumin, etc., will be less liable to reduce the Fehling's solution. (5) The delicacy of the test is not impaired by removing some of the solution in order to determine the end reaction. (6) If too much urine is added to one tube, the estimation can be carried out in the other tubes, thereby obviating the necessity of repeating the whole process.

We have had no practical experience with Beck's method, but it seems that considerable difficulty will be experienced in accurately dropping so small a quantity as four-twentieths c.c. into the tubes. It would be easier and more accurate to dilute the urine two or three times, and to use a burette in place of the pipette.

2. *Knapp's Method* is based upon the fact that mercury

cyanide in alkaline solution is converted into metallic mercury in the presence of sugar. The solution employed consists of 10 grammes of chemically-pure mercury cyanide and 100 c.c. sodium hydrate solution, specific gravity 1.145, to the litre (20 c.c. = 0.05 gramme glucose). Twenty c.c. of this solution are diluted with water to make 100 c.c. The solution is then heated to boiling, and urine, diluted as in Fehling's method, is added until the solution clears and the mercury settles to the bottom. After each addition the mercury is boiled. The end reaction is determined by placing a drop of the solution on filter paper and holding it first over a

FIG. 27.



Lohnstein's saccharimeter.

bottle of concentrated hydrochloric acid and then over one containing a saturated solution of hydrogen sulphide. A yellow spot should no longer appear. In the final calculation the number of c.c.'s of urine required divided into 5 equals the percentage of sugar present.

3. *Differential Density Method.*—The specific gravity of the urine is taken carefully, then some yeast is added, and after twenty-four to forty-eight hours the specific gravity is taken a second time. The difference between the two multiplied by 230

will then give the percentage of sugar. Stern has constructed a special uringlucosometer based upon this method. It requires one to two days before a positive result can be obtained, is very inaccurate and can hardly be recommended for ordinary use.

4. *Fermentation Test.*—The Einhorn tubes are generally employed, but since they are graduated very poorly, and one cannot tell when fermentation is completed, they should be discarded in favor of the more accurate Lohnstein saccharometer. This is essentially a U-shaped tube, open at both ends. The longer limb is closed during the process of fermentation by a ground-glass stopper. This stopper is provided with an air-hole, to which a similar hole corresponds in the drawn-out portion of the tube. The apparatus is filled with the urine, mixed with yeast, through the bulb A, while the two air-holes at B are in communication. The level of urine should be exactly at the zero mark. The stopper is then turned so that all communication is shut off, a little mercury is finally poured into the instrument and the whole placed into a vessel containing water at 35° to 40°, or into an incubator. After twelve hours fermentation will be complete, and the percentage of sugar can be read off. A test-tube accompanies the instrument, which enables accurate dilution. Sufficient water should always be added to the urine, so that the resulting mixture does not contain more than 1 per cent. sugar.

5. *Polariscopic Test.*—The use of the polariscope, as described on a previous page, is the quickest and most convenient way of estimating the percentage of sugar. Unfortunately, the instrument is too expensive for general use. If very accurate results are desired, the urine should be polariscoped twice, once before and once after fermentation, and the amount of levulorotation then added to the dextrorotation. Where acetone and diacetic acid are present, there is probably also some β-oxybutyric acid, which is decidedly levulorotatory, hence a double determination is absolutely necessary here.

Lactose.—Lactose gives a positive Trommer's and Nylander's test, but phenylhydrazine does not give an osazon, and fermentation does not begin until about twenty hours have elapsed.

A special reaction for milk-sugar is that of Rubner. The urine is boiled two or three minutes with an excess of lead acetate. If lactose is present, the urine turns yellowish-brown, and the precipitate dissolves in ammonia with a brick-red color. On standing, a cherry-red or copper-colored sediment falls to the bottom, while the supernatant liquid becomes clear and colorless. Dextrose will

give the same reaction, hence it should first be removed by fermentation.

Levulose.—Levulose reduces the solutions commonly employed and ferments, but turns the plane of polarized light to the left. For its detection Seliwanoff's test is used: 10 c.c. of urine are heated with resorcine and 2 c.c. of dilute muriatic acid, when a red color will appear.

Maltose.—Maltose behaves very much like glucose, but the crystals obtained on treating with phenylhydrazine have a different melting-point (207° C.).

Laiose (Leo's Sugar[1]).—On titrating a urine containing laoise, 1.2 to 1.8 per cent. more sugar will be indicated than by the polarimetric method. It is not as sweet as dextrose, does not ferment as actively and forms a well-characterized compound with phenylhydrazine. It does not give the Seliwanoff reaction.

Pentose.—Pentose is recognized by the following reaction: Three c.c. of urine are heated to boiling with 3 c.c. of hydrochloric acid (specific gravity 1.19) and a pinch of phloroglucin, when a cherry-red color will appear, which soon changes to greenish-black. Amyl alcohol will take up the pigment, and on spectroscoping the solution a band of absorption will appear between yellow and green. Instead of the above, Bial's reagent may be employed (Orcin 0.5, liquor ferri sesquichlorate 10 drops, acid muriatic concentrated 250 c.c.). A bluish-green pigment will separate out on boiling, which is also soluble in amyl alcohol.

Glycuronic acids also give the pentose reaction; the phloroglucin more readily than the orcin. In order to remove these, it is necessary to benzoylate 500 c.c. of urine, saponify the resulting ester with sodium ethylate and filter. A positive reaction in the filtrate can then only be due to pentose (v. Ahlftan).

Glycuronic Acids.—Glycuronic acid as such gives the pentose reaction, but since usually combined in the urine, slight differences in color are noted. Thus, with phloroglucin a more brown coloration is obtained, but the same band of absorption as pentose. The orcin reaction is only positive in case of menthol and turpentine-glycuronic acid, but the precipitate is violet instead of greenish-blue, unless spontaneous decomposition has set in and the acid is liberated. In a general way, glycuronic acid can be recognized by the history of the case and the odor of the urine. Thus, the patient may have taken chloral, camphor, naphthol, phenol, morphine, antipyrine, etc.; or an odor of peppermint may suggest

[1] See Virchow's Arch., vol. 107, p. 108.

menthol, or one of violets, turpentine and allied bodies. Trommer's and Nylander's tests are usually partially or completely positive. The plane of polarization is turned to the left, but to the right if the acid is set free by boiling with sulphuric acid. In this free state the phenylhydrazine, orcin and phloroglucine tests are positive, but fermentation is negative under all conditions.

Summary.	Trommer's or Fehling's React.	Nylander's.	Ferment.	Phenylhydraz.	Polarisc.	Orcin React.	Special Test.
Glucose	+	+	+	+ (melting point 205°C)	right	—	—
Levulose	+	+	+	+ (melting point 205°C)	left	—	Seliwanoff's reaction
Maltose	+	+	+	+ (melting point 207°C)	right	—	—
Lactose	+	+	negative in the first 20 hours	—	right	—	Rubner's reaction
Laiose	+	+	ferments slowly	+	no reaction or toward left	—	—
Pentose	+	+	—	+ (melting point 154—160°)	—	+	—
Glycuronic Acid	+	+	—	only the free acid	acid toward right salts toward left	+ (after splitting with acid)	—
Alkapton	+	—	—	—	—	—	see under "Alkapton"

Acetone.—Several c.c. of urine are treated with a few drops of 5 per cent. nitroprusside of sodium solution and strong sodium hydrate. In the presence of acetone, the red color will turn purple or violet when glacial acetic acid is added in excess. The test is more delicate if a large quantity of urine is distilled after the addition of some phosphoric acid and the first 10 or 20 c.c. are employed.

The following is somewhat more delicate: Several drops of Gram's solution and sodium hydrate are added to the distillate, when, in the presence of mere trace, the odor of iodoform will be evolved. Since this cannot always be detected readily, it is better to centrifuge the urine and to examine the sediment microscopically for the characteristic crystals.

Other tests for acetone, less commonly employed, are:

Reynolds' Test.—A small amount of the distillate is treated with freshly precipitated yellow mercuric oxide, prepared by precipitating mercuric chloride with sodium hydrate. In the presence

of acetone, black sulphide of mercury will form in the clear, filtered solution if a few drops of ammonium sulphide are added.

Denniges-Oppenheimer Test.—About 3 c.c. of urine are treated with a special reagent, drop by drop, until the precipitate formed no longer dissolves on stirring. The reagent is prepared as follows: Twenty grammes of concentrated sulphuric acid are poured into 100 c.c. of distilled water, then 5 grammes of freshly precipitated yellow mercuric oxide are added and the mixture set aside for twenty-four hours. When enough of the reagent has been added, the precipitate is filtered off, treated with about 2 c.c. more and 3 to 4 c.c. of a 30 per cent. solution of sulphuric acid, and placed in a vessel with boiling water. A slight cloud or precipitate will develop, depending on the amount of acetone present. Hydrochloric acid in excess will again clear up the fluid. Albumin will also give a precipitate, hence should be removed. The test is simple and delicate (1-20,000), and only possesses the disadvantage of also reacting with diacetic acid, since this yields acetone when treated with mineral acids. Fortunately, however, the significance of diacetic acid is the same as that of acetone.

Stock-Frohner Test.—If a small crystal of hydroxylamine hydrochlorate is dissolved in a few c.c. of the distillate, a blue color will be obtained if this is then treated with chloride of lime solution and extracted with ether. The test will be positive in a dilution of 1-1,000, but will also react with diacetic acid.

For quantitative purposes, 100 c.c. of urine are treated with 2 c.c. of 50 per cent. acetic acid, and distilled until only one-eighth remains behind. The distillate is then mixed with a carefully-measured quantity of one-tenth normal iodine solution (12.6 grammes iodine and 25 grammes potassium iodide to the litre). Usually 10 c.c. are employed for every 100 c.c. of urine. Sodium hydrate solution (50 per cent.) is then added in excess till all iodoform has separated out. The iodine in excess is precipitated with concentrated hydrochloric acid and retitrated, with a decinormal solution of thiosulphate of soda (24.8 grammes to the litre), until the fluid assumes a pale yellow color. A few c.c. of starch solution are then added, and the titration continued until the last trace of blue has disappeared. The amount of acetone in 100 c.c., in milligrams, can be determined by deducting the number of c.c. employed in titration from the total amount of iodine added and multiplying by 0.976.

Diacetic Acid.—*Gerhardt's Test.*—In the presence of diacetic acid, a few drops of ferric chloride solution will give a Burgundy

red color. The reaction should also be positive if the urine is treated with sulphuric acid and shaken out with ether, and the test repeated with this ethereal extract. The excretion of salicylic acid sometimes interferes, hence the urine should first be filtered through animal charcoal if salol, etc., has been taken.

Arnold's Test.—This test is, by far, the better, since it is more delicate, and does not respond to acetone and the various drugs. A 1 per cent. aqueous solution of para-amido-aceto-phenon is prepared and rendered colorless by the cautious addition of hydrochloric acid. Two parts of this solution are then mixed with one of a 1 per cent. solution of sodium nitrite and an equal volume of the urine to be tested. On adding ammonia, a brownish-red color will appear in all urines; but in the presence of diacetic acid, ten to twelve times the amount of pure hydrochloric acid will give rise to a beautiful purple color. After the addition of the ammonia, Lipliawski treats 0.6-2 c.c. with 15-20 c.c. of pure hydrochloric acid, 3 c.c. of chloroform and 2-4 drops of an aqueous solution of ferric chloride. A violet tinge will result if the tube is gently agitated.

β-Oxybutyric Acid.—The presence of β-oxybutyric acid manifests itself by a rotation toward the left after the sugar has been fermented with yeast.

The quantitative test is rather complicated, and depends upon the conversion of β-oxybutyric to a-crotonic acid. One hundred c.c. of urine are rendered feebly alkaline, and are then evaporated almost to dryness on a water-bath. The residue is transferred to a flask by means of 200 c.c. of 50 per cent. sulphuric acid, and distilled until 300 c.c. have been obtained, water being poured into the flask to keep up the volume. The distillate is extracted two or three times with ether, the ether distilled off and the residue heated on the sand-bath to 160° C., and dissolved on cooling with 50 c.c. of water. This aqueous solution of crotonic acid is now titrated with decinormal sodium hydrate solution, 1 c.c. of which corresponds to 0.0086 grammes of crotonic acid. By multiplying the result with 1.21, the amount of oxybutyric acid will be obtained.

Hemoglobin.—If a spectroscope is at hand, the urine should be acidified with acetic acid, and then examined for the characteristic absorption bands between D and E. Upon adding ammonium sulphide, reduced hemoglobin will form, which gives only one band, slightly beyond D. More often, however, the spectrum of methemoglobin will be obtained (one band between C and D, and another broader one between D and F). The chemical tests for

blood are used more often, since a good spectroscope is very expensive and the small, hand instruments are often unsatisfactory.

Heller's Test.—The phosphates are precipitated by rendering the urine strongly alkaline with sodium hydrate and boiling. In the presence of blood, the precipitate will show a bright red color, and the spectrum of hemochromogen may be obtained. In the absence of a spectroscope, the deposit is filtered off and dissolved in acetic acid, when the solution remains red in the presence of blood, but soon turns colorless, owing to oxidation. The test is very delicate, since one part in 4,000 can still be detected with ease.

Guajacum Test.—If equal parts of tincture of guajacum and old ozonized oil of turpentine be allowed to float on urine containing blood-coloring matter in solution, a white ring will form which gradually turns blue. The urine should be acid in reaction. Instead of turpentine, peroxide of hydrogen may be used. The test is very delicate, but pus will sometimes give the same ring; this disappears, however, on heating, while that caused by blood does not.

Aloin Test.—Instead of tincture of guajacum, a 3 per cent. solution of aloin in 60-70 per cent. alcohol may be employed in the same way, mixed with oil of turpentine. A beautiful red color will appear at the zone of contact.

Donogany's Test.—Ten c.c. of urine are treated with one c.c. of a solution of ammonium sulphide, and the same amount of pyridine, when an orange color will appear in the presence of blood. If doubt exists, the spectrum of hemochromogen should be looked for. If the ammonium sulphide and pyridine are not fresh, the color obtained will be green or brown, changing to yellow on the addition of ammonia.

Melanin.—On adding ferric chloride, a black precipitate appears in the urine in the presence of melanin, which is soluble in sodium carbonate and can be reprecipitated with mineral acids. Bromine water will also give a precipitate which rapidly becomes black.

Bile Pigment.—Gram's iodine solution is diluted ten times with alcohol and then layered over a few c.c. of urine in a test-tube, when a green ring will form at the line of junction in the presence of bile (Smith's test).

Instead of the above, urine may be floated over some nitric acid containing a trace of nitrous, made extemporaneously by heating pure nitric acid with a small piece of wood, until red fumes are given off. A play of colors will then be obtained at the zone of

contact, of which the green is most characteristic (Gmelin's test). The urine may also be filtered and a drop of the acid applied to the filter-paper (Rosenbach's test).

Huppert precipitates 10 to 20 c.c. with milk of lime or barium chloride. The precipitate is filtered off and then brought into a beaker by perforating the filter and washing with a small amount of alcohol, acidulated with sulphuric acid. The mixture is boiled, when in the presence of bile, the solution will turn emerald-green. The test is very delicate, but not as easily performed as some of the others.

A very delicate test has been recommended recently by A. Jolles.[1] Ten c.c. of urine are mixed in a test-tube with 2 to 3 c.c. of chloroform and 1 c.c. of a 10 per cent. solution of barium chloride. The mixture is then centrifuged, the fluid above the chloroform and precipitate poured off, and the tube filled with distilled water, shaken and centrifuged a second time. In case of dark-colored urines, this is repeated a third time. After the water is decanted, the chloroform and precipitate are shaken with 5 c.c. of alcohol, and then two or three drops added of an iodine solution, which is prepared as follows: 0.63 gramme of iodine and 0.75 gramme of corrosive sublimate are each dissolved separately in 125 c.c. of alcohol, poured together, and then 250 c.c. of pure hydrochloric acid added. In the presence of even faint traces of bile, a distinct green color is obtained. The reaction can be hastened by placing the test-tube in hot water for a few minutes. Indican and hemoglobin do not interfere with the reaction. The presence of one-tenth milligram of bilirubin in 100 c.c. of urine still gives a positive result. Where the above tests are negative, a few drops of blood may be drawn and centrifuged in a capillary tube. In the presence of bile, the clear supernatant fluid will be tinged yellow, often before the bile appears in the urine.

Bile Acids.—Bile acids are always present when bile pigments are found, so that separate tests are unnecessary. The test generally employed is that of Pettenkofer. Solutions of bile acid or their salts exhibit a brilliant cherry red color, changing on standing to a deep purple, when treated with concentrated sulphuric acid after the addition of a few drops of a 25 per cent. solution of cane sugar. The temperature of the mixture should be kept as low as possible, and an excess of sugar should be avoided on account of the danger of producing caramel.

Pathological Urobilin.—Ten to 20 c.c. of urine, which is usually

[1] Deutsch. Arch. f. klin. Med., vol. 78, Nos. 1 and 2.

orange-colored with yellowish foam, are extracted with chloroform by shaking and the extract then treated with a few drops of dilute Gram's solution. On further adding dilute sodium hydrate, the chloroform extract will turn yellow and exhibit a beautiful green fluorescence.

In the presence of mere traces, the urine must be extracted with amyl alcohol, and the alcoholic extract then treated with a concentrated solution of zinc chloride in spirits of ammonia. In the presence of urobilin there will be a greenish fluoresence and an absorption band between C and F.

Occasionally urobilin may be found in the blood before it has appeared in the urine. About 1.5 c.c. of blood are drawn from the finger and mixed with the same amount of 1-1,000 calc. oxalate solution. The tube is then placed in the centrifuge and the clear fluid poured off. An equal amount of 10 per cent. zinc acetate solution is added and the mixture again placed in the centrifuge. The supernatant fluid is then examined for the fluorescence and spectrum bands.

The use of zinc acetate has also been recommended for the urine by Schlesinger,[1] since it is much more delicate than the chloride and does not require the addition of ammonia. Furthermore, bilirubin and other pigments are precipitated, and do not interfere. The urine is simply mixed with an equal amount of 10 per cent. solution of zinc acetate in absolute alcohol and filtered, when the filtrate will exhibit the fluorescence, especially when the rays of light are concentrated upon it with a convex lens.

Fat.—Fat in urine is easily identified under the microscope as highly refractive globules, which stain black with osmic acid. If a quantitative analysis is desired, the urine may be extracted with ether and the ether then evaporated.

Leucin and Tyrosin.—In order to examine for leucin and tyrosin, the urine must be concentrated on the water-bath to about one-tenth its original volume, and then treated with an equal amount of alcohol. After standing a short time, the sediment should be examined for the characteristic crystals. Sometimes it is necessary to first precipitate the urine with lead acetate, filter, and remove the excess of lead with sulphuretted hydrogen. The crystals, when present, can be further identified as follows: The sediment is filtered off, washed with water, dissolved in ammonia, to which a little ammonium carbonate has been added. The solution is allowed to evaporate, when the tyrosin remains behind.

[1] Deutsch. med. Woch., Aug. 6, 1903.

A few crystals are moistened with a few drops of concentrated sulphuric acid, covered, and set aside for half an hour. They are then diluted with water, heated and while hot, saturated with calcium carbonate, and the solution filtered. The filtrate will assume a violet color when heated with a few drops of very dilute chloride of iron. For identifying leucin, the sediment is treated with a small amount of alcohol, in which leucin is more soluble than tyrosin. The alcohol is then allowed to evaporate and a portion of the residue treated upon platinum foil with nitric acid, when a colorless residue is obtained, which forms an oily droplet when heated with a few drops of sodium hydrate solution.

Cystin.—Cystin can be recognized by its characteristic crystals. If the sediment does not contain these crystals, the urine should be strongly acidified with acetic acid and examined a second time. Frequently an odor of hydrogen sulphide is noticed after the urine has stood for some time.

Alkapton.—The presence of alkapton will cause reduction of Fehling's solution, but not of Nylander's. Ammoniacal silver solution is reduced in the cold and ferric chloride gives a temporary, bluish-green color. If treated with Millon's reagent, a yellow precipitate will slowly form, gradually turning to orange. On heating, the color of the precipitate readily changes to light terra-cotta red. Upon exposure to air, the urine will turn reddish-brown. Phenylhydrazine, fermentation, polariscopy and the pentose reagent will give negative results. Urines containing phenol or melanin may also turn dark on standing, but these bodies can be recognized by their special tests.

Diazo Reaction.—For the diazo reaction, Ehrlich employs two solutions: one containing 5 per cent. hydrochloric acid and 1 per cent. sulphanilic acid, and another containing 0.5 per cent. sodium nitrite. The two solutions are mixed in the proportion of 40:1 immediately before using. It is most convenient to use a long, narrow cylindrical graduate which is filled up to 2.5 c.c. with the sulphanilic acid solution. One drop of sodium nitrite solution is then added with a dropper, and then urine up to the 5 c.c. mark. By means of a pipette, a few c.c. of ammonia water are then floated upon the mixture. With every urine, a colored ring will form at the line of contact, but while the hue is orange or reddish-brown under ordinary circumstances, it is distinctly crimson or garnet-colored if the reaction is positive. If the graduate be now shaken (this should never be done with the thumb, but with a stopper, since typhoid urine frequently contains typhoid bacilli), the foam

will also be a decided red. Furthermore, the mixture may be poured into a porcelain basin containing much water, when a beautiful salmon color will be obtained. Ehrlich states that on standing a green precipitate will form in the alkalinized mixture, but this is only the case if the reaction is strongly positive.

Dimethylamidobenzaldehyde Reaction.—A few cubic centimeters of urine in a test-tube are treated with five to ten drops of a 2 per cent. solution of dimethylamidobenzaldehyde in equal parts of water and concentrated hydrochloric acid; the mixture is set aside or agitated for a few minutes and the color then noted. The reaction is positive, if a distinct cherry-red develops.

Skatoxyl.—A few c.c. of urine are treated with hydrochloric acid and diluted chloride of lime solution, just like for the indol reaction, but instead of chloroform, amyl alcohol is added. On shaking the test-tube (this must be done very carefully as the amyl alcohol emulsifies easily) a brown color will be imparted to the amyl alcohol, due to skatoxyl. Some of the color will also, as a rule, be taken up by chloroform and will color this pink.

Phenol.—Millon's reagent (mercury, one part; fuming nitric acid, one part; water, two parts) will give a brick-red precipitate on boiling. Furthermore, ten c.c. of urine may be boiled in a test-tube with a few c.c. of nitric acid. On cooling, some bromine water is then added. A pronounced turbidity or a precipitate indicates the presence of phenol. A few drops of sodium hypochlorite gives a blue color, and if heated with iodine and sodium hydrate solution a red, amorphous precipitate forms. Whenever an appreciable quantity of phenol is present, chloride of iron will give a violet or greenish color. If it is desired to test for other substances which give the same reaction, the phenol must first be removed by shaking out with ether after the fluid has been rendered strongly alkaline with sodium carbonate.

Rosenbach's Reaction.—A number of years ago, Rosenbach described the following reaction: If nitric acid is added drop by drop to boiling urine, the urine will turn burgundy-red with bluish-red foam. With more nitric acid, the color will change to yellowish-red and yellow. By adding ammonia, a bluish-red precipitate will form which will dissolve in an excess with brown color. The reaction seems to be due to the oxidation of indican and skatol and possesses the same significance as the test for these.

Lactic Acid.—The urine is evaporated on a water-bath to a thick syrup and extracted with 95 per cent. alcohol. This is decanted after twenty-four hours, evaporated to a syrup, acidified

with dilute sulphuric acid and extracted with ether till this no longer reacts acid. The ether is then distilled off and the residue dissolved in water and tested as usual for lactic acid.

Volatile Fatty Acids.—For the quantitative estimation of acetic, formic, etc., acids, a certain amount of *fresh* urine is distilled with sulphuric acid and the distillate then titrated with decinormal sodium hydrate solution. The only other acid which might distil over is benzoic acid, but this is of little consequence. The result is expressed in the same number of c.c. of decinormal sulphuric acid. The identification of the various acids requires an elaborate chemical analysis.

Gases.—If hydrogen sulphide is suspected, a strip of filter-paper moistened in sodium hydrate and lead acetate solution is held over the urine. After a varying length of time this will be colored black if the gas is present.

Ptomaines.—The poisonous diamines which may occur in the urine are isolated as follows: The urine of twenty-four hours is shaken with a 10 per cent. solution of sodium hydrate and benzoyl chloride until the odor of the latter has disappeared. The precipitate is filtered off and digested with alcohol The filtered alcoholic extract is concentrated to a small volume and poured into about 30 times the amount of water. After twelve to forty-eight hours, the benzoylated diamines separate out in white crystals.

Drugs.—*Lead.*—A strip of bright magnesium wire is placed in the urine. Ammonium oxalate is then added to the fluid in the proportion of 1:150. In one hour or sooner, a gray coating will be noticed on the magnesium, which can be further identified as lead by washing and drying and finally heating with a crystal of iodine. A yellow stain will show the presence of lead or cadmium. The latter can be disregarded.

Mercury.—Five c.c. of egg albumin are rubbed up in a mortar with the same amount of saturated salt solution and dissolved in 500 c.c. of urine. The fluid is then heated upon a water-bath until all the albumin has coagulated. The precipitated albumin is collected upon a filter, dried and rubbed up in a mortar with 10 c.c. of muriatic acid. Then 40 c.c. more of acid are added and the mixture set aside in a beaker in which a copper spiral has been suspended. After twenty-four hours the spiral is washed with cold and hot water, alcohol and ether, and dried in the air. It is then introduced into a dry glass tube closed at one end. At the upper end of the spiral a small crystal of iodine is sublimed by heating, finally the entire glass tube is gently heated. The mercury will

also sublime and form a brick-red ring of iodide of mercury on the inside of the tube. The width of the ring will be proportioned to the amount of mercury present. The test is very delicate, for it will be positive in the presence of 0.0005 gramme mercury.

Arsenic.—One c.c. of urine is mixed with 4 c.c. dilute sulphuric or muriatic acid and a piece of chemically pure zinc. The test-tube is closed with a cotton plug and covered with a piece of filter-paper moistened with concentrated silver nitrate solution. In the presence of arsenic, a lemon-yellow color will develop which will soon turn black.

Iodides.—Ten to 15 c.c. of urine are shaken with 5-10 drops of concentrated, yellow nitric acid and 1-2 c.c. chloroform. In the presence of iodine, the chloroform will turn violet and the addition of thiosulphate of soda will again cause the color to disappear. With the usual indican tests, a violet color is also generally obtained.

Bromides.—Bromides can be detected with the above tests since free bromine will tinge the chloroform brown. Or the urine may be heated with a small amount of sulphuric and chromic acids. In the presence of bromine, a piece of filter-paper saturated with fluorescin solution and held over the flask, will turn red. If iodine is also present in the urine, this latter must be treated with sulphuric acid saturated with the fumes of nitric acid. By shaking with carbon disulphide, the iodine can then be removed.

Chlorate of Potash.—Ten to 15 c.c. of urine are warmed with one-fourth its volume concentrated hydrochloric acid, when a play of colors from red, bluish-violet, yellow to colorless will be observed. If much chlorate is present, free chlorine may escape.

Chrysophanic Acid appears in the urine after the use of rhubarb, senna, chrysorobin and cascara sagrada. The color of the urine is generally yellowish, turning to red upon the addition of alkali and again disappearing when acidified with acetic acid. With the indican test, the chloroform will be tinged green and Nylander's solution will be reduced.

Santonin.—Santonin gives the same reactions as chrysophanic acid, but is insoluble in ether. If the urine is shaken out with ether, a few drops of sodium hydrate added to the extract will not change the color.

Salicylic Acid.—A few drops of chloride of iron will color the urine dark red to bluish-violet. Antipyrine and phenacetine may give similar reactions. Muriatic acid should then be added to the urine tested as above until a red color is still visible. On now

shaking with acetic ether, the red color will disappear entirely if due to salicylic acid.

Antipyrine.—Chloride of iron will give a dark red color which does not disappear on boiling (differentiation from diacetic acid) or shaking with acetic ether (differentiation from salicylic acid). A ruby-red crystalline sediment will appear if the urine is treated with a drop of muriatic acid and Lugol's solution.

Phenacetine.—Chloride of iron will give a brownish-red color; two drops of muriatic, two drops of a 1 per cent. sodium nitrite solution, some soda lye and alkaline aqueous α-naphthol solution will give a red color, which turns violet if more muriatic acid is added.

Copaiba.—Muriatic acid will give a pink color, which will become violet on boiling. See also under albumin tests.

Urotropine.—Urine containing urotropine will turn yellow if treated with bromine water. The precipitate is soluble in an excess of urine.

Chloroform.—Fehling's solution will be positive. If the urine is distilled on a water-bath in a stream of carbonic acid, the distillate will give off a disagreeable odor of phenylisocyanate if heated with aniline oil and alcoholic potash lye.

Sulphonal and Trional.—In order to detect hematoporphyrin, 20-25 c.c. of urine are precipitated with a solution consisting of equal parts of saturated barium hydrate and 10 per cent. barium chloride. The precipitate is collected on a filter, washed with water and alcohol, then mixed with a few drops of muriatic acid and a small amount of alcohol. After a few minutes the mixture is warmed on a water-bath and filtered. The reddish filtrate, if spectroscoped, will give two absorption bands, one before D, and the other between D and E.

Morphine.—The urine will give Trommer's test and turn polarized light to the left (morphine glycuronic acid). But it may also be dextrorotatory owing to the presence of glucose, or give the orcin reaction for pentoses.

Tannic Acid gives a black color with tincture chloride of iron.

Turpentine.—The urine smells of violets and turns polarized light to the left (turpentine glycuronic acid).

Orthoform.—Chromic acid will give a dark red color.

Pyramidon.—The urine has a distinct pink color, which can be dissolved out by means of ether, chloroform or amylic alcohol.

Naphthaline gives a blue fluorescence with a few drops of ammonia. Another test is to add to 6 c.c. of urine, 4 drops of chloride

of lime solution and a few drops of hydrochloric acid. The urine becomes yellow, and if shaken out with ether the color can be extracted. If this ether is layered over a 1 per cent. resorcin solution and rendered alkaline with a few drops of ammonia, the resorcine is colored a blue-green; with nitric acid, the color will be cherry red.

Resorcin gives the above test directly.

CHAPTER VII.

RENAL AND BLADDER STONES.

According to their chief constituents, renal and bladder stones are subdivided into those consisting of

1. *Urates* (chiefly free uric acid, acid urate of sodium and less frequently, urate of ammonia).
2. *Phosphates* (chiefly the phosphates of calcium and magnesium and carbonate of calcium).
3. *Oxalates* (calcium oxalate).
4. Cystin and xanthin.
5. Mixed stones.

GENERAL PROPERTIES.

Color.—Uratic stones are yellow to dark brown; phosphatic stones, grey or greyish-yellow. Those consisting of oxalate of lime are reddish-brown or black, but the smaller ones frequently appear white or grey. Stones consisting of cystin are colored pale yellow; those of xanthin, light brown.

Surface.—A warty (mulberry) surface is characteristic for oxalic stones; uratic stones are less rough and the others of the list generally smooth.

Consistency.—Cystin stones are frequently as soft as wax; phosphatic stones, brittle and chalky, oxalic stones are the hardest of all, then come the uratic stones.

CHEMICAL EXAMINATION.

The calculus is divided into two halves by means of a scroll saw. The surface is then washed off in water, so that the nucleus and layers come clearly to view. A portion of the nucleus and each layer is then scraped off and examined separately. If the stone is not layered, but is uniform in structure, it is simply pulverized in a mortar. A small sample of the powder is heated on a platinum foil.

1. The powder burns up almost entirely and the amount of ash remaining behind is slight. Such stones consist of uric acid, urates, xanthin or cystin. Urates and xanthin will burn without flame and will give off an odor of prussic acid; cystin burns with a

bluish flame and odor of sulphurous acid.. For more accurate analysis, a second sample of the powder is evaporated to dryness in a porcelain dish with a few drops of nitric acid. If the residue gives a purple color with ammonia and violet color with lye (murexid test), the powder contains uric acid or urates. If the powder leaves no residue on heating to red heat, it is pure uric acid; if ammonia is evolved on treating some of the original powder with soda lye we are dealing with the ammonium salt. The other urates will leave a slight residue on heating to red heat. Xanthin is present if the murexid test with ammonia is negative, but if soda lye will give a beautiful red color. Cystin reacts neither with ammonia nor with soda lye, but is readily soluble in ammonia. On slowly evaporating the latter, characteristic hexagonal plates will form.

2. The powder does not burn up, but blackens and leaves considerable residue. It may then consist of phosphates, carbonates or oxalates. A small portion of the powder is carefully warmed with dilute muriatic acid, which will dissolve the greater portion. We now cool, filter, dilute with water and add ammonia until strongly alkaline. A precipitate may consist of

(a) Phosphate of lime or magnesia.
(b) Triple phosphate.
(c) Oxalate of lime.

The precipitate is now separated from the fluid by centrifuging and then shaken with acetic acid. Earthy phosphates and triple phosphate will dissolve, while oxalate of lime will remain behind and can be identified under the microscope. The filtered solution is then tested as follows: 1. On adding ammonium molybdate and nitric acid and warming up to 60° C., a yellow precipitate will indicate the presence of phosphoric acid. 2. The other half of the filtrate is then treated with soda lye; the resulting precipitate is examined microscopically for amorphous or crystalline earthy phosphates or for crystalline triple phosphate.

If no precipitate has been obtained on adding ammonia to the solution of the powder in hydrochloric acid, the stone must consist of calcium or magnesium carbonate. If muriatic acid be dropped on the stone, carbonic acid gas will then be evolved. Oxalate of ammonia is added to half of the ammoniacal solution; a precipitate of oxalate of lime will indicate the presence of calcium. The other half is treated with sodium phosphate, when a precipitate of triple phosphate will occur in the presence of magnesia.

The portion of the stone insoluble in muriatic acid should be tested for uric acid (murexid test).

CHAPTER VIII.

MICROSCOPICAL EXAMINATION OF URINE.

Every physical and chemical examination of urine should be supplemented by a thorough microscopical examination, for which purpose a good compound instrument with low and high-power lenses is absolutely essential.

When time is not pressing, the urine may be allowed to sediment in a conical glass for a few hours; the deposit is then sucked up by means of a long pipette and a drop of it examined on a slide with a cover-slip, first with a low, then with the high power. It is always, however, better to centrifuge the urine with an instrument run by hand or water-power or by electricity. The latter generally have the highest speed and one to three minutes will suffice to completely throw down the suspended matter. For accurate work it is best to combine sedimentation with centrifuging. The urine is poured into a conical glass, after a sufficient amount has been removed for the chemical tests, and is allowed to settle for several hours; the sediment is then sucked up and centrifuged. For still more accurate work, the entire quantity of twenty-four hours is allowed to settle after a piece of camphor or a crystal of thymol has been added to prevent decomposition (chloroform is often recommended, but is undesirable since it settles to the bottom and mixed with the deposit; formaline is also undesirable, since it interferes with some of the chemical tests). In such cases the sediment may be more abundant and it will be necessary to examine more than one slide.

Frequently difficulty will be experienced in completely clearing the urine by means of the centrifuge. This may be due to the presence of mucus, bacteria or urates. Thick, mucinous urine can be easily rendered thin by digesting the urine for several hours in a warm place with a pinch of pancreatin and bicarbonate of soda. A turbidity caused by uric acid or urates will readily dissolve on warming, but will reprecipitate unless the sediment is examined at once on a warm slide. Frequently, too, the sediment will be so abundant that finer elements, such as casts, are entirely obscured. If the urine has been alkaline and the deposit consists chiefly of phosphates, the addition of a few drops of acetic acid will cause

these to disappear. In the case of urates, simple warming will generally suffice, while with excessive pus the sediment must be diluted.

The following is a list of elements which may occur in urine (the more common ones are in italics):

A. CRYSTALLINE OR AMORPHOUS ELEMENTS.

(a) IN ACID URINE.

1. *Uric acid.*
2. *Sodium* or *potassium urate.*
3. *Calcium oxalate.*
4. Primary calcium phosphate (only when very acid).
5. Secondary calcium phosphate. } only when slightly acid.
6. Tricalcie or trimagnesic phosphate. }
7. Triple phosphate.
8. Calcium sulphate.
9. Leucin and tyrosin.
10. Hippuric acid.
11. Xanthin.
12. Soaps of lime and magnesia.
13. Bilirubin.
14. Hematoidin.

(b) IN ALKALINE URINE.

1. Secondary calcic phosphate.
2. Tricalcic or magnesic phosphate.
3. *Triple phosphate.*
4. Calcic carbonate.
5. *Ammonium urate.*
6. Indigo
7. Cystin.

B. FORMED ELEMENTS.

1. *Epithelial cells.*
2. *Pus cells.*
3. *Red blood cells.*
4. *Casts.*
5. Parasites and bacteria.
6. Tumor particles.
7. Spermatozoa.
8. Fat.
9. Vegetable matter, hairs, cotton fibres, grass, pollen, etc.

Uric Acid.—This often crystallizes in whetstone form, the crystals occurring either singly or in the form of rosettes, composed of long, narrow slabs with rounded ends. Dumbbell-shaped crystals, larger than those of calcium oxalate, are also seen occasionally. The crystals are the largest which are found ordinarily in the urine; they form the so-called brick-dust or lateritious deposit so often seen in cold weather, and their characteristic red color is due to uroerythrin. They dissolve readily on heating and by the addition of alkalies, and the murexid test is characteristic.

A deposit of uric acid does not necessarily mean an excess of

this substance in the urine, nor are the crystals always thrown down if an excess is present.

Sodium and Potassium Urate are always amorphous and colored. The fine granules may be so abundant that they obscure the entire field and coat formed elements (structures resembling coarsely granular casts) may sometimes be seen. They dissolve on warming, and the addition of acids will precipitate uric acid in form of whetstone crystals or rhombic plates.

Calcium Oxalate.—Crystals of calcium oxalate belong to the most characteristic elements found in urine. They form diamond-shaped octahedra, which are colorless, highly refractive and rarely attain a large size. One or two opposite axes may be elongated. Dumb-bell forms may be seen made up of two bundles of needle-like crystals united in the form of the figure 8. They are usually associated with or adherent to casts and differ from similar uric acid crystals, in that they are radially striated, shorter and thicker and lack the characteristic color. According to Simon there is also an amorphous variety. Alkalies and acids do not affect the crystals. The diagnosis of oxaluria should never be made from the presence of the crystals, even when they are abundant.

FIG. 28.

Calcium phosphate crystals. (Musser.)

Primary Calcium Phosphate (**Monocalcium Phosphate**) occurs rarely together with uric acid in strongly acid urines. The crystals resemble uric acid, but are colorless and readily soluble in acetic acid.

Secondary Calcium Phosphate and tricalcic and magnesic phosphate are very rare in acid urines, but common in alkaline. They generally do not form characteristic crystals by transparent granules, like the urates, but colorless. They do not disappear on

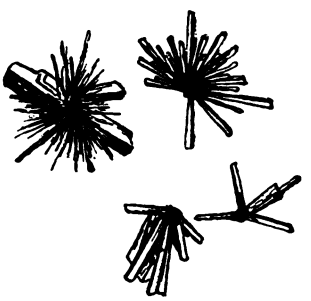
FIG. 29.

Crystalline phosphates. (Finlayson.)

heating, but are readily dissolved on adding acetic acid. Rarely acicular, star-shaped crystals are observed; or, in the case of magnesia, highly refractive plates.

Triple Phosphate (**Ammonia-Magnesium Phosphate**) is also very rare in feebly acid urine, but common in alkaline. The crystals

FIG. 30.

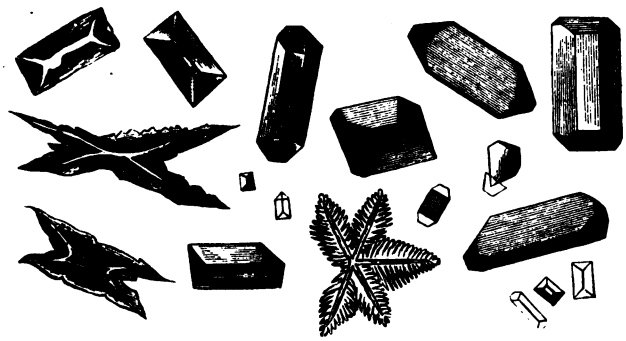


Monocalcium phosphate crystals.

are usually large rhombic prisms of coffin-lid shape, but smaller ones may be mistaken for calcium oxalate. Their solubility in acetic acid will, however, prevent this error. In alkaline urines, there may be in addition a variety of star-shaped, "snow-flake" crystals, with four, five or more arms and feathery borders.

Calcium Phosphate has only been observed in a few cases. The reaction here is strongly acid. The crystals appear as long, color-

FIG. 31.

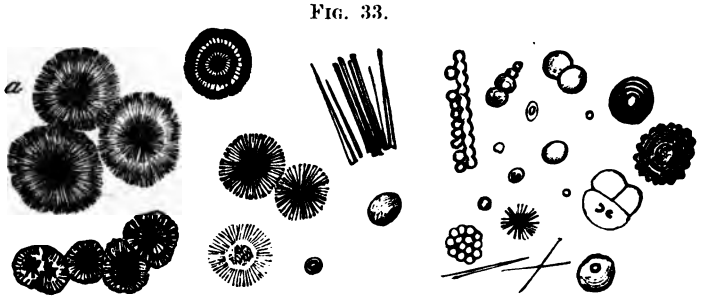


Various forms of triple phosphates. (Finlayson.)

FIG. 32.

Calcium sulphate crystals. (v. Jaksch.)

FIG. 33.

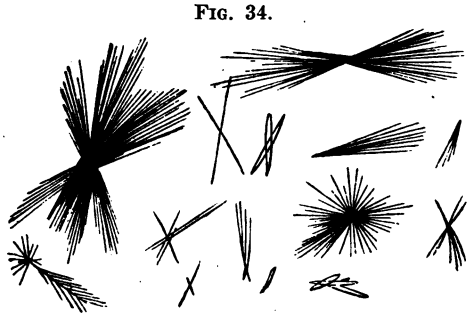


Crystals of leucin (different forms). (Crystals of kreatinin-zinc chloride resemble the leucin crystals depicted at *a*.) The crystals figured to the right consist of comparatively impure leucin. (Charles.)

less needles or elongated prismatic tablets which do not dissolve in acids or ammonia.

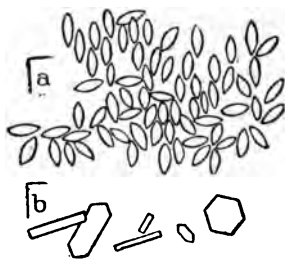
Leucin and Tyrosin.—Leucin occurs in form of spherules of variable size which closely resemble fat, but can be easily dis-

FIG. 34.



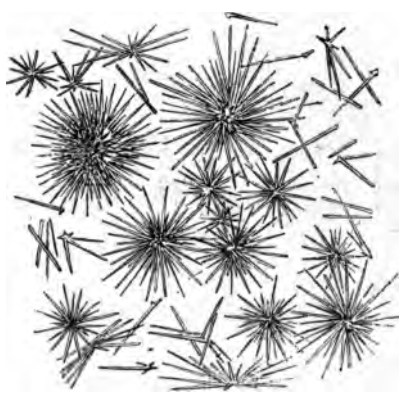
Tyrosin crystals. (Charles.)

FIG. 35.



a, Crystals of xanthin (Salkowski); *b*, Crystals of cystin. (Robin).

FIG. 36.



Lime and magnesium soaps. (v. Jaksch.)

tinguished by their insolubility in ether, their brown color and the presence of concentric striations and fine radiating lines. **Kreatinin** zinc chloride closely resembles certain types.

Tyrosin appears as very fine needles, usually grouped in bundles, crossing each other at various angles. They are insoluble in acetic acid, but soluble in ammonia and hydrochloric acid.

Xanthin crystals closely resemble some of the colorless crystals of uric acid.

Soaps of Lime and Magnesia.—Calcium and magnesium salts of

FIG. 37.

Calcium carbonate crystals.

certain higher fatty acids are of very rare occurrence. They closely resemble tyrosin in appearance, but do not give the reactions of this substance.

Bilirubin forms yellow or red rhombic plates in icteric urine. They dissolve in alkalies and chloroform, but not in ether and give the usual bile reactions.

FIG. 38.

Ammonium urate crystals.

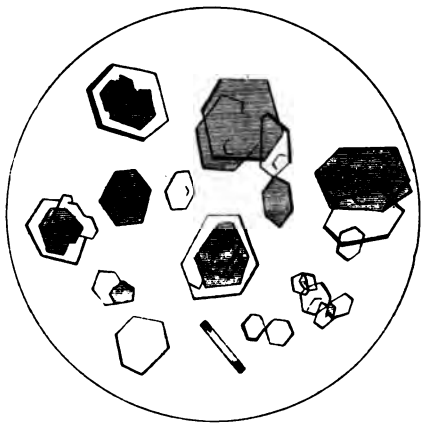
Hematoidin is also very rare and can hardly be distinguished from bilirubin. It has been encountered in various diseases of the kidney and bladder, attended with bleeding.

Calcium Carbonate appears under the microscope in the form of minute granules, occurring singly or arranged in masses. Dumb-

bell forms also occur. They are easily identified by the evolution of gas on addition of an acid.

Ammonium Urate is characteristic of ammoniacal fermentation.

FIG. 39.



Crystals of cystin spontaneously voided with urine. (Roberts.)

The crystals cannot be mistaken for anything else; they are generally spherical, amorphous, brown in color and beset with

FIG. 40.

Crystals of cholesterin. (Musser.)

spicules, but may also appear as delicate needles arranged into a spherical body. They are dissolved by acid with the subsequent separation of characteristic crystals of uric acid.

Indigo occurs as delicate blue needles, or as amorphous granules in urines that have undergone decomposition. Their presence is probably the result of bacterial decomposition of indican. Rarely calculi consist almost entirely of indigo-blue.

Cystin occurs in the form of colorless, hexagonal plates, which are soluble in ammonia and hydrochloric acid and insoluble in acetic acid, water, alcohol and ether. When heated, they burn with a bluish-green flame without melting.

Cholesterin is rarely found in the form of large, flat, colorless plates, with ragged edges. Frequently one corner appears punched out.

B. Formed Elements.

Epithelial Cells.—It may not be amiss to review briefly the characteristics of the epithelial lining of the genito-urinary tract.

Fig. 41.

Epithelial cells from the pelvis of a human kidney. (Rieder.)

In the convoluted tubules, the cells are but little larger than leucocytes with polyhedral cell body, but in the descending loop of Henle they become flatter and more squamous in type. The ascending limb presents similar but somewhat higher cells, while in the distal convoluted portion and the collecting tubules, the cells gradually assume a cylindrical shape and increase in height with the width of the tubule.

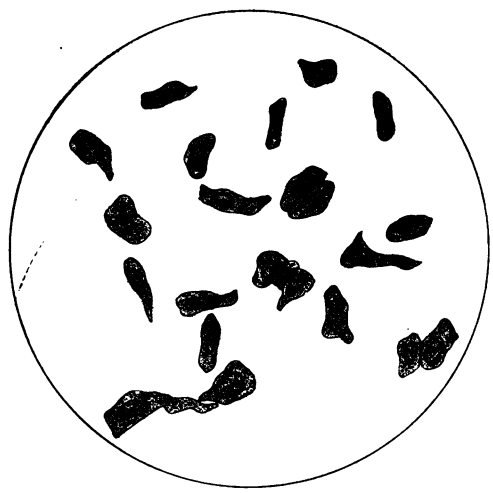
In the renal pelvis and ureters, the cells are of a transitional

type, that is, cells which rapidly change from the columnar of the deeper layer to the stratified scaly of the superficial. In the pelvis the superficial cells frequently have a distinct process which makes them appear conical or caudate.

The epithelium of the bladder so closely resembles that of the ureter and pelvis that it is often impossible to distinguish between the two. At the neck of the bladder, the cells may also be caudate, but the processes generally have a greater length.

In the female urethra the lining is generally stratified squamous, but may be simple columnar. In the prostatic portion of the male urethra, the epithelium resembles that of the bladder; in the mem-

FIG. 42.



Epithelial cells from the human ureter. (Rieder.)

branous division it gradually passes into the stratified columnar variety, which in the spongy part is transformed to a simple columnar epithelium. In the fossa navicularis and the glans, the stratified squamous type is again encountered.

The vagina is lined by large flat elements which are very characteristic.

From this it may be seen that while there may be considerable difference in appearance between renal and vaginal cells, the lining cells of the intermediary tract do not differ so widely that their probable origin can be determined by their size and shape. Added to this is the fact that the urine always changes the shape of the cells to some degree, and finer structures, such as the striations

of the renal cells, are never preserved. Some claim that the identification of the epithelial cells of the different portions of the genito-

FIG. 43.

FIG. 44.

Epithelial cells from the mucous membrane of the human bladder. (Rieder.)

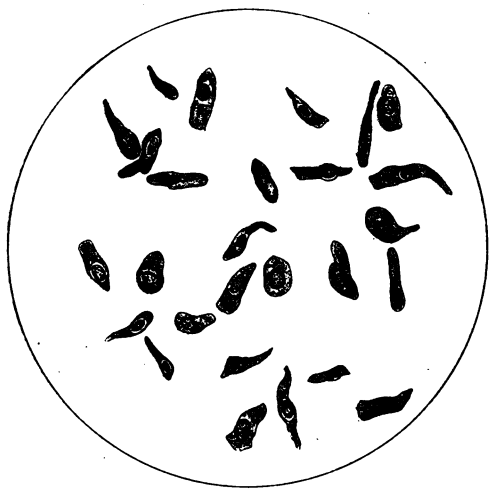
Fig. 43.—From the urinary sediment from a case of cystitis. The cells are somewhat swollen after maceration in the altered urine.

Fig. 44.—Removed from the internal surface of a normal bladder.

urinary tract is an easy task, and even go so far as to locate the portion of the kidney affected in renal disease, but the careful

examination of many thousands of sediments and comparison with clinical history and symptomatology has convinced us that such differentiation is based chiefly on imagination.

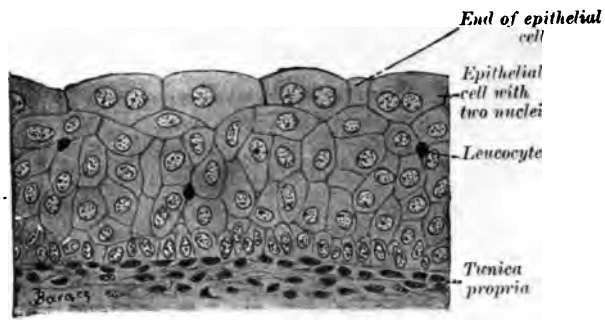
FIG. 45.



Epithelium from the human male urethra. (Rieder.)

For practical purposes, we may divide the epithelial cells commonly encountered in sediments, into three types: 1. Round. 2. Caudate. 3. Flat cells. Round cells are usually derived from the

FIG. 46.



From a section through the mucous membrane of an ape's urinary bladder. × 300.

uriniferous tubules or the deeper layers of the mucosa of the pelvis or lower genito-urinary tract. They are round or cubical, slightly larger than a leucocyte, but with distinct, vesicular nucleus and

very sharp contours. Frequently the protoplasm shows fatty degeneration. A diagnosis of "renal epithelium" is only admissible, if albumin and casts are also present (especially if the cells adhere to the casts), or if the cells occur in typical strings, like in the uriniferous tubules. If found with considerable pus but without casts or more than traces of albumin, a pyelitis is possible, especially if the cells are joined in a shingle-like manner. But it must never be forgotten that similar elements occur in the deeper layers of almost the entire genito-urinary tract from the pelvis down, and that a diagnosis in the absence of other characteristic elements is extremely hazardous.

An important observation on renal cells, is that of Quincke.[1] In a case of unilateral hydronephrosis, the sediment was rich in cells, 24-36 mikra in diameter, with their entire cell body filled with very coarse granules, disappearing after the addition of acetic acid. These elements were probably epithelial cells derived from the straight tubules, altered by pressure; since they were subsequently found in similar cases, they are of diagnostic value and indicate that a slow atrophy is in progress.

Renal cells may occur in all diseases of the kidney, but are especially marked in the desquamative types. If they contain droplets of fat, it may be possible to determine the existence of a degenerative process.

2. **Caudate Cells.**—Cells with a distinct conical process are generally derived from the pelvis of the kidney or the neck of the bladder. The statement that caudate cells are pathognomonic of pyelitis is passed from one text-book to the other, yet there are few of us who would risk a diagnosis on the so-called caudate cells that are seen in the urine of pyelitis. There is as yet no simple microscopic method of differentiating between cystitis and pyelitis.

3. **Flat Epithelium** belongs to the normal ingredients of urinary sediment, especially in women where the desquamation of vaginal elements is often so active as to obscure everything else. The cells are usually large, polygonal and provided with a well-defined nucleus, and the extra-nuclear protoplasm is usually transparent. In order to distinguish vaginal cells from those of the bladder, etc., the urine should be drawn off with a catheter, moreover the vaginal cells often occur in sheets. A large number of flat epithelial cells in the male (or in the catheterized specimen of the female) if not accompanied by much pus, will speak for a catarrhal process of the ureters, bladder or urethra. In the latter two instances the increase is much more marked than in the former.

[1] Deutsch. Arch. f. klin. Med., vol. 79. Nos. 3 and 4.

The so-called mucous corpuscles of normal urine are nothing but young vesical epithelial cells.

Leucocytes.—A few pus cells may be encountered in any normal urine and their quantity is often increased in men due to an old gonorrhea, or in women as a consequence of a vaginal discharge. Larger amounts indicate disease of the genito-urinary tract, but the appearance of the cells alone will not disclose their origin. If derived from the kidney, pus and other casts, and small epithelial cells may be present; and the amount of pus is usually small except in abscess, if from the pelvis, the urine is acid and may also contain caudate cells, while in cystitis, the reaction is often alkaline (except in typhoid and colon cystitis) and phosphates are frequently present.

For the diagnosis of urethral pus, Thompson's two-glass test is often employed, that is, the patient is instructed to pass the first part of his urine into one glass and the second in another. In gonorrhea or other catarrhal conditions of the urethra, only the first glass will be cloudy and contain pus cells.

The largest amounts are seen in pyonephrosis and after the rupture of a neighboring abscess into some part of the genito-urinary tract, where almost pure pus may be excreted. In acid and feebly alkaline urine, the cells are usually well preserved, but in very alkaline urine or when the pus comes from an old abscess, it is often impossible to identify the individual corpuscles, which may even be converted into a gelatinous mass. In such cases the following reaction for pus may be employed: The urine is acidified with acetic acid, filtered, and the contents of the filter treated with a few drops of tincture of guajacum, when in the presence of pus the filter-paper will be colored blue.

Occasionally it is important to enumerate the number of pus-cells contained in the urine. For this purpose, the ordinary Thoma-Zeiss blood counter is employed, very dilute acetic acid being added to the urine if necessary. In general, 5,000 cells to the cubic millimeter signify a mild cystitis, and in severe cases 50,000 and more may be counted. With many pus cells a trace of albumin will occur in the urine, even in the absence of renal disease. This applies to the filtered as well as to the unfiltered specimen, since some of the albuminous principles of the cells always go into solution.

Red Cells may occur normally in the urine of women from admixture with menstrual blood; they may also be present in small amounts as a result of catheterization or after the passing of

sounds. Usually, however, red cells point to a distinct pathological process somewhere in the genito-urinary tract. If from the kidneys, the amount is usually small and intimately mixed with the urine, the individual corpuscles often appear as "shadows" and epithelial and blood casts are also present. Common conditions associated with renal hematuria are the severer types of infectious diseases, hyperemia of the kidneys in circulatory disturbance, acute and to a less extent, chronic nephritis, stone of the kidney, carcinoma or tuberculosis, and, more rarely, renal abscess and aneurism, embolism or thrombosis of the renal vessels. As compared with hemoglobinuria, hematuria is of much more common occurrence. Certain poisons (carbolic acid, cantharides, etc.) may also be responsible for the presence of blood in the urine.

Blood coming from the ureter or renal pelvis is difficult to identify, but often long coagula are passed, and there may be other signs which point to pelvic or ureteral disease.

In vesical hematuria the admixture is a less intimate one, and the cells have preserved their normal appearance and rapidly settle unless ammoniacal fermentation has set in. Large, irregular clots may also be voided. Hematuria may be found with severe cystitis, tuberculosis or tumor of the bladder, foreign bodies, or parasites.

In case the blood is derived from the urethra, after trauma, the first portion of the urine voided will contain blood, but not the second.

Urine containing blood will be bright red or more brown. If recent, the individual cells can generally be readily identified by their size, their pale yellow color and sharp contours. Often, however, they are considerably altered by the urine and may appear crenated or entirely devoid of color (blood-shadows). In such cases it may be necessary to resort to one of the chemical tests for blood.

A peculiar form of hematuria has been described by Senator as "renal hemophilia." It does not seem to be associated with distinct pathological lesions, and occurs chiefly in neurasthenia.

Like with pyuria, both the filtered and unfiltered specimens will contain traces of albumin in the presence of blood.

Casts.—The most important morphological structures occurring in urine are casts, and every specimen should be most carefully examined for these. There is still considerable doubt as to their method of formation, but they probably consist of albumin and are formed in the convoluted tubules, where they may frequently be discovered in situ on hardening and cutting the kidneys of cases of nephritis.

Their significance is in the main the same as that of renal albumin, but they tell us more, since their appearance, to a certain extent, will disclose the severity of the renal lesion. Then, too, they may be frequently found where albumin, even in traces, is absent (especially in the very chronic types of interstitial nephritis) so that the microscopical examination may enable a diagnosis of nephritis, where the chemical tests have failed. Conversely, renal albuminuria may exist without the presence of casts especially in renal congestion, essential albuminuria, or where a cystitis is also present and ammoniacal decomposition has destroyed the delicate structures. It is a mistake, however, to believe that

FIG. 47.

Hyaline casts from a case of acute nephritis; 1, plain hyaline cast; 2, granular deposit on hyaline cast; 3, cellular deposit (blood and epithelium). (Musser.)

casts invariably mean a nephritis. Personally, the writers have frequently encountered typical hyaline casts in the urine of patients who presented no renal symptoms and where the subsequent history, extending over years, removed all doubts as to the presence of a nephritis. In persons of advanced years, a scant number of hyaline or even finely granular elements, in the absence of albumin, need cause no alarm, as they are often only a manifestation of slight thickening of the renal vessels. In the opinion of one of our foremost clinicians, they may even be regarded as a blessing, as they will enforce certain precautions in diet and general living. (Plate IV.)

Casts must never be confounded with pseudo-casts or cylindroids,

PLATE IV.

FIG. 1.

1. Hyaline Casts with Granular Matter and Epithelial Cells deposited upon them. 2. Amyloid (waxy) Cast. (Musser.)

(Oc. 4, Ob. D.) Drawn by J. D. Z. Chase.

FIG. 2.

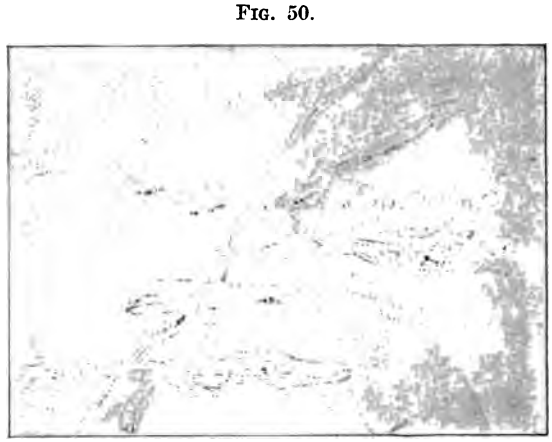
Blood Casts from Case of Acute Nephritis. (Musser.)

(Oc. 4, Ob. D.) Drawn by J. D. Z. Chase.

Hyaline casts are colorless, very pale and transparent. In the presence of bile, they may be tinged yellow. They are best seen with the high power and flat mirror, without condensor and with the iris diaphragm partly closed. Their structure is generally homogenous, their borders parallel and ends rounded. In thickness and length they vary considerable, probably with the portion of the uriniferous tubule where they originate, and it is always best to specify their size. Sometimes the ends are broken off obliquely or are spirally elongated and the body may be notched. Their identification is facilitated by the addition of Lugol's solution, picric acid or fuchsin solution to the sediment.

Finely granular casts have a distinctly granular surface, which

FIG. 50.



Cylindroids. (Musser.)

permits them to be identified more readily than hyaline casts. Coarsely granular casts are still more easily visible and frequently possess a yellow color. Their granules are probably derived from the breaking down of renal epithelium cells and consequently they indicate a more serious lesion than the hyaline structures.

Epithelial, pus or blood casts are made up almost entirely of cells, or else the cells merely adhere to their surface. They are seen only in severe lesions and are not of common occurrence. All transition stages between hyaline, granular and cellular casts may occur.

Waxy casts differ from hyaline casts in that they possess a higher degree of refraction, a yellow or yellowish-gray color, are usually not attacked by acetic acid, and give the amyloid reaction (mahog-

PLATE V.

Concretions of Chronic Prostatitis. (Taylor.)

PLATE VI.

Amyloid Bodies in the Prostatic Tubules shown on Transverse Section. (Taylor.)

any color with Lugol's solution, which turns to a dirty violet on adding dilute sulphuric acid. They may also have granules and cells adherent to their surface, but not as often as hyaline casts. Frequently, not entire casts, but only broken pieces are encountered. They do not always signify amyloid disease of the kidneys and amyloidosis is not necessarily accompanied by the excretion of amyloid casts.

Cylindroids resemble tube-casts in that they are colorless and cylindrical, but are less refractive, longer, striated and often twisted so that their differentiation, as a rule, is easy. They probably consist of mucus and may be encountered in almost every urine.

FIG. 51.

Spermatozoa from urine. (Musser.)

Spermatozoa.—Spermatozoa are best seen with the higher powers and are easily recognized by their conical head and long tail. If found in male urine after intercourse or nocturnal emission, they possess no significance. Their constant presence may be noted in certain pathological conditions of the seminal passages, with spinal diseases and in true spermatorrhea, due to masturbation or venereal excess. The presence of spermatozoa in the urine of little girls may be of great medico-legal importance. (Plates V. and VI.)

Where spermatozoa are present, other characteristic elements may be found, such as large, rounded cells, with distinct nucleus, which enclose spermatozoa and delicate, cylindrical bodies of homogenous, hyaline structure which are derived from the spermatic

canals and have been termed "testicular casts." In diseases of the prostate, numerous small shiny granules, the so-called lecithin-granules, are sometimes seen, together with rounded and angular bodies of concentric structure (corpora amylacea) and star-shaped or elongated crystals of spermin. In pure prostatic secretion, these will show very readily if a 1 per cent. solution of ammonium phosphate is added, but this is not the case with urine.

Tumor-particles.—In papillomatous or carcinomatous tumors of the renal pelvis or bladder, small tumor-particles may be voided

FIG. 52.

Secretion of chronic prostatitis, showing granular phosphates, degenerated cylindrical epithelial cells, and pus. (Taylor.)

spontaneously, but such occurrence is certainly very rare. Suspicious sheds should be fixed, hardened, cut and stained the usual way for identification. Usually the particles will turn out to be mucus or blood-clot.

Fat is readily identified as small, highly refractive granules, readily soluble in ether. It is often present accidentally but may be due to parasites lodged in the genito-urinary tract (chyluria).

Other Elements.—Various animal parasites may from time to time be encountered in the urine. The most common of these are: (1) *Trichomonas vaginalis,* which is derived from the vagina and occasionally gives rise to hematuria. (2) ***Bilharzia hematobia.***

The eggs are oval, 0.16 mm. long and 0.05 mme. broad, and are provided with a distinct spike-like projection which issues from one extremity or the side. They can be seen with the low power and are most frequently found in the last bloody drops of urine voided. (3) *Filaria.* Filaria embryos may be found in the urine

FIG. 53.

in cases of filarial chyluria. They should be looked for in the coagulum, a bit of which is teased out and pressed between two slides. Cases are common in Egypt, but very rare in the United States. (4) *Echinococcus* hooklets and fragments of cysts. The former can be easily identified under the microscope, the latter give

FIG. 54.

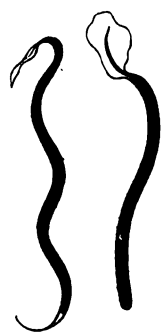
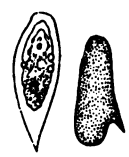


FIG. 55.



the chitin reaction. (5) *Amœbae.* (6) *Eustrongylus gigas.* (7) *Distoma hematobium.* These three are very rare. (8) Occasionally the eggs of intestinal parasites accidentally contaminate the urine.

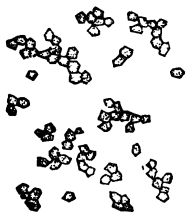
Concerning bacteria, see special chapter.

Starch cells and lycopodium grains are not infrequent in females who use dusting powder. The former are oval, concentrically striated and turn violet on the addition of iodine solution. The

FIG. 56.

Corn starch.

FIG. 57.



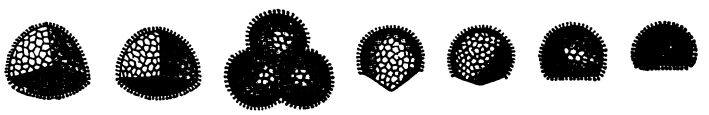
Rice starch.

FIG. 58.

Wheat starch.

pollen grains of lycopodium appear as sphero-tetrahedonal bodies, the surfaces being reticulated and the edges beset with short projections.

FIG. 59.



Lycopodium.

Foreign bodies of all description may be seen in the urine in hysteria. Care should also be taken to keep the urine in clean receptacles, since many admixtures, bacterial and otherwise, may be derived from the sediment contained in bottles. Cotton fibres are universal.

CHAPTER IX.

BACTERIOLOGY OF URINE.

The urine as it leaves the kidneys and as it is stored in the bladder, is practically a sterile fluid in healthy individuals. If collected aseptically with a catheter and passed into a sterile receptacle, it may remain unaltered for a long period, but during the normal act of urination there will almost always be an admixture of germs from the meatus of the urethra and the glans, which may eventually spoil the urine.

In order to examine a urine for micro-organisms, the sediment may be employed for direct microscopical inspection or for cultures. In the latter case, particular care should be exercised to avoid outside contamination. The urine is drawn off by means of a sterile catheter into a sterile flask, allowed to settle, and a portion of the sediment then transferred upon suitable media by means of a sterile pipette. Sometimes it is advisable to keep the urine in an incubator for twenty-four hours before making culture, so as to allow the germs to proliferate. For simple microscopical examination such aseptic precautions are not necessary, as outside contamination, if present, will be so slight as to escape detection. A few drops of the centrifuged sediment are simply spread on a glass slide and allowed to dry, the slide is then passed through the flame of the Bunsen burner several times until hot to the touch, in order to coagulate the albumin and fix the morphological elements so that they do not wash off during the subsequent staining. Sometimes the urine itself does not contain sufficient fixative, when a drop of very dilute egg-albumin must be added.

In the following conditions a bacteriological examination may be necessary for a diagnosis:

Tuberculosis of the genito-urinary tract.
Gonorrhea.
Sepsis.
Typhoid fever.

An examination will be desirable, though not essential, in all suppurative conditions of the genito-urinary tract or wherever pus is present.

Tuberculosis.—In tuberculosis of the bladder and kidney, the urine frequently contains blood, pus and tubercle bacilli. If the lesion is located in the bladder, the entire urine will be altered, but in unilateral renal disease it is desirable to examine the two samples obtained by ureteral catheterization in order to determine the affected side. (Plate VII., Fig. 1.)

In order to demonstrate tubercle bacilli, the urine should be drawn off by means of a catheter to avoid contamination with smegma bacilli, which resemble the tubercle bacilli in their morphology and staining properties. Where the urine contains much mucus and pus, so that it cannot be well sedimented, a pinch of pancreatin and bicarbonate of soda may be added, since this will digest the heavy ropy masses in a few hours.

Tubercle bacilli are stained as follows: The fixed slide or slides (in suspicious cases it is always best to prepare three or four) are placed on two glass rods, resting on the ring of an ordinary iron stand, which must be absolutely level. They are then flooded with carbol-fuchsine (saturated alcoholic solution of fuchsine, 10 per cent., 5 per cent. carbolic acid 90 per cent., the mixture should be at least a day old) and heated directly with the Bunsen burner until steam is given off. This is repeated in a few minutes, then the specimens are allowed to slide into a glass dish by raising one glass rod. They are then washed off in water by lifting them from the dish with a forceps and then go into 5 per cent. sulphuric acid for about half a minute. After washing in water, decolorization is completed by leaving in 95 per cent. alcohol for a few minutes. The alcohol is finally washed off and the slides counterstained for a minute or two with very dilute methylene-blue. They should be examined with the oil-immersion lens, when tubercle bacilli will be readily identified as slender, straight or slightly curved rods. They occur singly or two or three individuals lie side by side or end to end. While all cells and other bacteria appear blue, they alone have retained the red dye.

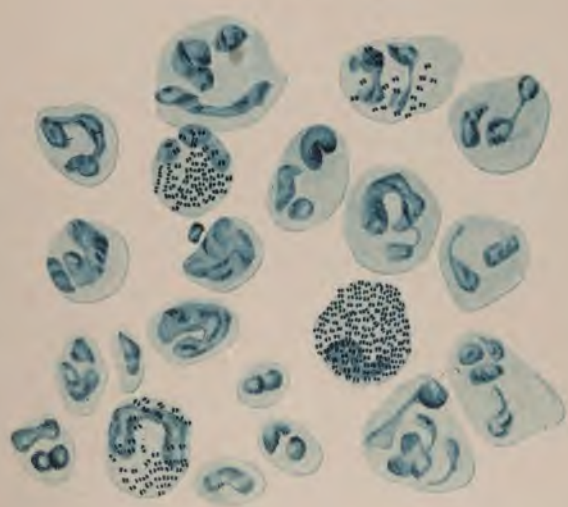
As stated above, the smegma bacillus may occasionally appear like the tubercle bacillus, and special precautions are necessary, as it may even occur in urine directly drawn from the bladder. The smegma bacillus is, however, never grouped like the tubercle bacillus and never beaded. Furthermore, it is completely decolorized by leaving the slides in absolute alcohol for five to eight hours after they have been in the acid. The staining of the tubercle bacillus is not affected by this. Recently Pappenheim's modification has been recommended, since with it the smegma bacillus is

PLATE VII.

FIG. 1.

Tuberculous Sputum Stained by Gabbett's Method. The Tubercle Bacilli are seen as Red Rods, all else is Stained Blue. (Abbott.)

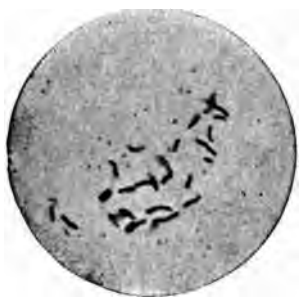
FIG. 2.



Gonococcus. (Musser.)

less liable to be stained. The slide is prepared the same way and then heated with a solution consisting of fuchsine, 1 part, 5 per cent. carbolic acid 100 parts, absolute alcohol, 10 parts. The excess of staining fluid is drained off, when the preparations are immersed from three to five times in Pappenheim's solution, care being taken to let the fluid drain off slowly after each immersion. The stain consists of one part of corallin (rosolic acid) in 100 parts of absolute alcohol, to which methylene blue is added to saturation. The mixture is further treated with 20 parts of glycerine and is then ready for use. The specimens are finally washed in water and dried. The tubercle bacilli will be red, everything else blue.

FIG. 60.



Smegma bacilli, similar in appearance to tubercle bacilli. × 1000 diam. (Park.)

If repeated examinations by above methods are negative, the fresh sediment may be injected into the abdominal parietes of a guinea-pig. In from three to six weeks the inguinal lymph nodes will swell and tubercles will develop in the spleen, liver and other internal organs.

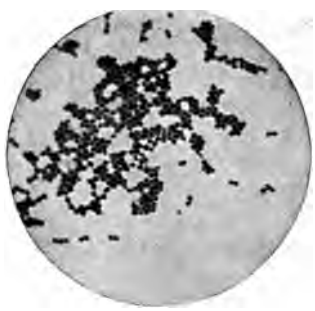
The cultivating of tubercle bacilli is hardly possible with urinary sediments, since the slowly-growing bacillus would be rapidly overgrown by other germs present.

Gonococcus.—For the diagnosis of gonorrhea, it is always best to obtain a drop of the secretion from the meatus or after massaging the prostate, since the cocci rapidly die off in the urine. Sometimes, however, only the urine is at our disposal, when the sediment should be dried and fixed as stated above. For ordinary purposes, a 1 per cent. solution of methylene blue or Jenner's stain is best for gonococci, which appear as small, oval, coffee-bean shaped granules, grouped as twos or fours within the pus or epithelial cells. For more accurate differentiation, Gram's modi-

fied stain should be used, as follows: The fixed slides are stained one to two minutes in 10 parts of saturated alcoholic solution of gentian violet to 90 parts of a 5 per cent. solution of carbolic acid. Without washing they are then transferred for one to three minutes into Lugol's solution (one part of iodine, two parts of potassium iodide and 300 parts of distilled water) and again without washing into absolute alcohol for about one and one-half minutes, or until no more color is given off; they are then washed and counterstained with Bismark-brown. (Plate VII., Fig. 2.)

Recently neutral red has been employed for the staining of gonococci. A small drop of fresh pus or sediment is mixed with a loop-ful of saturated aqueous solution of neutral red, diluted 100 times in normal salt solution, and examined in a hanging drop.

FIG. 61.



Staphylococcus. × 1100 diameters. (Park.)

FIG. 62.

Streptococci in peritoneal fluid, partly enclosed in leucocytes. × 1000 diameters. (Park.)

Intracellular gonococci will then be stained deep red, while other germs do not take up the dye.

Chronic gonorrhea often manifests itself by the presence of so-called "gonorrheal-threads," consisting of pus cells held together in a matrix of mucus. Though undoubtedly gonorrheal in origin, it is generally very difficult to demonstrate gonococci in these shreds.

Gonococci are very difficult to grow from urinary sediment, since they frequently have died off. From the secretion, however, an abundant growth may often be obtained, if it be remembered that gonococci require uncoagulated human serum for their propagation. It is merely necessary to mix ordinary agar with sterile hydrocele or ascitic fluid and to inoculate the surface of a slant.

In *sepsis* germs will often be excreted in the urine, especially

when the bacteriological examination of the blood has been negative. The organisms which most commonly concern us here are staphylococci, streptococci and colon bacilli, less frequently pneumococci, proteus, etc. Their isolation and identification requires the usual bacteriological technique.

Typhoid Fever.—The examination of urine of cases suspicious of typhoid fever is of the greatest importance, since the germs are excreted in about 30 per cent. of the cases, and often where the Widal and other signs fail. It is true that blood-cultures give as high as 80-85 per cent. positive results, but the elaborate technique necessary for venepuncture argues against its general use by the practitioner. One should not, however, be misled by the mere

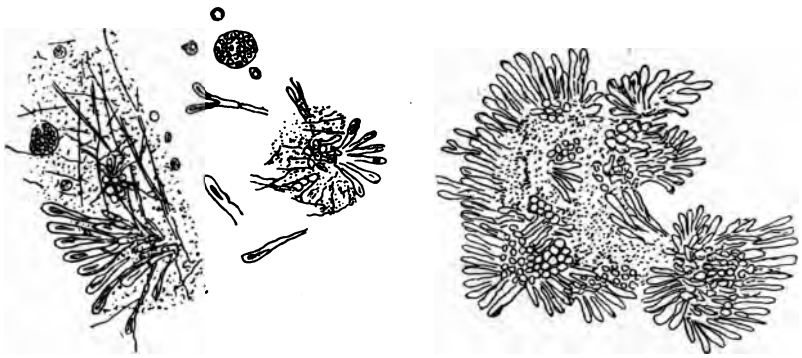
FIG. 63.

Colon bacilli. Twenty-four-hour agar culture. × 1100 diameters. (Park.)

presence of motile, Gram-negative bacilli in the urine, since even in typhoid fever these will often be colon bacilli. In bacteriological laboratories, where all the necessary media are at hand, the quickest and safest way of identifying typhoid bacilli in urinary sediment is by means of the method of Drygalski-Conradi, originally recommended for the feces. The liquefied culture-medium (consisting of peptone, salt, nutrose, sugar of milk, krystal violet, litmus and agar) is poured into three sterile Petri dishes and allowed to harden. A loopful is then spread over the surface of plate one with a special glass rod; plates two and three are then inoculated with the same spreader and all three placed in the incubator. After twenty-four to thirty-six hours the colon bacilli will form red, opaque colonies, while the typhoid colonies are much smaller, trans-

parent and blue, like dew-drops. This different behavior is due to the fact that the colon bacillus will split up the sugar of milk with the formation of acid, which colors the litmus red, while the typhoid germ cannot attack the sugar, but will decompose the proteids with the formation of alkali. The suspicious typhoid

FIG. 64.

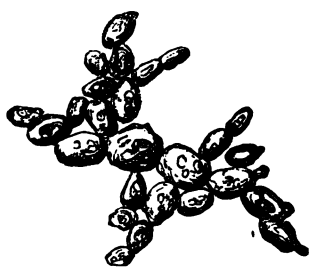


Actinomyces.

germs may further be tested with an animal immune serum of high agglutinating power.

For the ordinary practitioner, however, this method is too complicated. There is as yet no simple method to distinguish between both germs, since both have the same morphological appearance

FIG. 65.



Yeast cells.

and are Gram-negative. The colon bacillus, however, ferments glucose broth, reduces neutral red agar and forms indol, which properties are not shared by the typhoid bacillus.

The germs usually encountered in suppurative disease of the genito-urinary tract are the various types of staphylococcus, the

streptococcus and particularly the colon bacillus. The former two may be readily identified by methylene blue or by Gram's stain, and can be grown on the usual media.

Actinomyces kernels may be observed in the urine when the disease in question has attacked the genito-urinary tract, or when the organism has found its way in the urine from other organs.

Yeasts and moulds are sometimes found in diabetic urines, but may also occur in the absence of sugar.

Urines which have undergone ammoniacal fermentation frequently contain the so-called *Micrococcus ureæ* in large quantities. This germ forms long chains, like the streptococcus, but the individual members of the chain are considerably larger. It is responsible for the decomposition of urea into ammonia.

CHAPTER X.

PRESERVATION OF URINE.

GENERAL ROUTINE EXAMINATION OF URINE.

A number of drugs have been recommended for the preservation of urine, but the best is thymol. A few crystals may be put into the bottle, which is given to the patient, and the urine may then be kept for a long time before it spoils. Instead of thymol, camphor or a few drops of an alcoholic solution of salicylic acid may be employed. The great disadvantage of chloroform lies in the fact that it settles to the bottom and mixes with the sediment. Recently formalin has been recommended, but C. Strzyzowski[1] concludes that this substance is unsuited since it interferes with too many important reactions. Thus, urea will combine with formalin to form a leucin-like deposit. Uric acid will also form a compound and the indican reactions will be faint or absent altogether. The behavior toward albumin varies; sometimes traces are no longer precipitated on boiling preserved urine. The influence upon sugar, pentose, glycuronic acid, acetone, diacetic and β-oxybutyric acid is very slight, while bile-principles may be precipitated with the urea, from which they can be dissolved out by acid alcohol. Pettenkofer's reaction is no longer possible in the presence of formalin.

No matter what the preservative, especial care must be taken with the sugar reaction, and several tests should be used as control.

For the preservation of organized sediment, the following solution is recommended[2]:

Sodium chloride	1 gme.
Sodium sulphate	5 gme.
Mercuric chloride	0.5 gme.
Distilled water	200 gme.

The sediment is treated with this solution for twenty-four hours. The fluid is then poured off and the sediment washed a few times with distilled water. All constituents will appear in their unaltered shape and structure, just as they are found in the urine. To

[1] Therap. Monatshefte, May, 1904.

[2] Pharmac. Centralhalle, 1895, p. 484.

prepare specimens, a small amount is taken up with a pipette and mounted in glycerine. Instead of above solution, formalin may be employed.

With every sample of urine obtained by the physician, the color, transparency, reaction and specific gravity should be noted. About 30 c.c. are then filtered through paper, if necessary with the aid of talcum, Fuller's earth, magnesia or charcoal. The rest is set aside in a conical glass and allowed to sediment. The filtrate is distributed among three test-tubes: (a) a large one which is filled about one-sixth full, (b) a medium-sized one, filled about two-thirds, and (c) a small one, filled about one-fourth. To (a) about one-tenth of *Nylander's solution* is added. A black precipitate on boiling = sugar; (b) is boiled only in its upper portion; a precipitate which is dissolved on the addition of a few drops of *acetic acid* = excess of *phosphates;* a precipitate or turbidity which does not dissolve, but becomes more distinct on the addition of acetic acid = *albumin.* If the turbidity is at all marked, or an actual precipitate has formed, some urine should be filtered into an Esbach tube up to the mark U, then *Esbach's reagent* up to R. After shaking, the tube is set aside for twenty-four hours, when the amount of precipitate = *percentage of albumin.* To the urine in test-tube (c) (which must be acidified with acetic acid, if not normally acid) a pinch of *sulphosalicylic* acid is added; a turbidity or precipitate will be referable to *albumin,* and will serve as control test for the heat and acetic acid reaction. It is always well to gently heat this test-tube if the reaction was positive, as *urates* and *albumoses,* which may also be thrown down, will then dissolve, while the albumin precipitate will become more pronounced.

Whenever the Nylander test is positive, other tests should be employed as control, as many substances other than sugar also give a partial or complete reaction. A portion of the urine (unless very pale) is then precipitated with lead acetate, filtered and *polariscoped,* another portion is mixed with fresh yeast and poured into the *Lohnstein saccharometer* (the inaccurate Einhorn instrument should be entirely discarded). Dextro-rotation in the polariscope and the formation of carbon-dioxide gas in the saccharometer, are positive proof that *sugar* is present and furthermore enable a quantitative analysis. The amount of sugar may, however, be so small that both tests give doubtful results, then recourse should be had to the *phenylhydrazine test.* When a polariscope is not at hand, and a rapid result is desired, the urine may be titrated with *Fehling's* or *Rudisch's* solutions. Where Nylander's

reaction is partially or completely positive, but the other tests enumerated above, all or in part negative, the following principles may be present:

Albumin, owing to the formation of bismuth sulphide. The albumin should first be removed by boiling the acidified urine and filtering.
Pentose—detected by orcin test.
Glycuronic Acid— } The patient's history should be investigated.
Drugs— }
Chrysophanic acid.—The patient has taken rhubarb, senna, cascara, etc., and the urine is usually dark red.
Melanin.—Urine is dark or becomes dark on exposure and reacts positive to special tests for melanin.
Hydrogen sulphide.—Detected by odor and special test.

The following table will show, in a general way, when it is desirable to test for other principles:

1. *Chlorides*—
   Pneumonia and other acute febrile diseases (proportionate to the general severity of the case and often when exudates form. At the crisis and often a few hours before the appearance of other symptoms of improvement, the chlorides are sharply increased.
   Acute and chronic renal disease (diminished).
   Carcinoma of stomach (diminished). With the resorption of exudates and transudates (increased).
   To detect digestive power of patients (10—15.0=normal, less =below normal).
2. *Phosphates* (rarely required)—
   Pneumonia and acute infectious diseases, acute and chronic nephritis, like chlorides, phosphatic diabetes (increased).
3. *Sulphates* (rarely required)—
   Acute febrile diseases (increased, but decreased during convalescence).
   Conjugate sulphates increased in intestinal putrefaction from coprostasis, due to carcinoma of the intestines, with diminished excretion of acid in stomach and in obstructive jaundice.
   Neutral sulphur increased in cystin diathesis.
4. *Urea and Total Nitrogen*—
   Diseases of liver (acute yellow atrophy, cirrhosis, carcinoma (diminished).
   Diseases of kidney (especially where tubules are affected), (diminished).
   Acute febrile diseases, especially those ending by crisis (increased).
   Diabetes mellitus (increased).
   Conditions associated with dyspnea (increased).
   Congestion of kidneys with concentrated urine (increased).
5. *Ammonia* (rarely required)—
   Acute yellow atrophy and other hepatic disease, phosphorus poisoning, fevers, dyspneic conditions and diabetes (increased).
   Nephritis (diminished).
6. *Uric Acid and Xanthin Basis*—
   Gout (increased before the attack, diminished after; often inconstant).
   Leucemia and other diseases associated with leucocytosis (increased).
   Nephritis (diminished).

7. *Albumose*—
   Where there is accumulation with more or less absorption of pus in the body.
   Ulcerative lesions of the intestines.
   Scurvy, pernicious anemia, leukemia and other disorders of blood.
8. *Bence Jones Albumin*—
   When there is suspicion of multiple bone tumors.
9. *Hemoglobin*—
   With dark color of urine, after ingestion of poisons and with severe infectious diseases.
10. *Indican*—
    Carcinoma of the stomach and gastric conditions associated with hypo or anchlorhydria.
    In obstruction of the small intestines (not in simple constipation).
    In empyema, putrid bronchitis or gangrene of lung.
11. *Skatoxyl*—like indican.
12. *Rosenbach Reaction*—like indican.
13. *Phenol*—
    Like indican and after poisoning with carbolic acid and allied compounds.
14. *Bile*—
    Where color of urine is dark brown, especially if foam is colored.
    Diseases of liver, pancreas and bile ducts.
    Severe infections and poisoning.
15. *Urobilin* (not important)—
    Pernicious anemia.
16. *Melanin* (not important)—
    Where urine is dark in color.
    In suspected melanotic tumors.
17. *Alkapton* (not important)—
    Where urine is dark in color.
18. *Diazo reaction*—
    Typhoid, miliary tuberculosis.
    Measles.
19. *Ehrlich's Dimethylamidobenzaldehyde Reaction*—
    Wherever there is increased katobolism of tissue albumins, especially in tuberculosis.
20. *Acetone*—
    Diabetes (especially before coma), in prolonged fevers, in pregnancy and conditions of cachexia, especially carcinoma of stomach.
21. *Diacetic Acid*—like acetone.
22. *β-oxybutyric Acid*—like acetone.
23. *Leucin and Tyrosin*—
    In diseases of the liver, notably in acute yellow atrophy.
24. *Cryoscopy*—
    In renal disease, wherever there is suspicion of renal insufficiency.

When the chemical examination is completed, the sediment should be collected, centrifuged and examined on a slide with a cover-slip. Where a bacteriological examination is also required, a portion of the centrifuged sediment is spread out as thin as possible on a slide, allowed to dry, fixed and stained as described in a previous chapter.

Calculi or gravel, if present, should be collected on a filter and subjected to a chemical analysis as described in Chapter VII.

After ureteral catheterization, or with infants, only small quantities of urine may be available. With only 5 c.c. the procedure would be as follows: The entire quantity is first centrifuged, and a small amount of the sediment removed and examined microscopically and, if necessary, bacteriologically. After the color, appearance and reaction have been noted, the specific gravity is determined by means of Saxe's instrument (page 32). The entire quantity is then taken and divided into two halves, one for the Nylander sugar test, the other for the determination of albumin. The ring test is preferable here, since it will also give an approximate idea as to the presence and amount of indican, bile, etc., present. Should the observation of E. Reiss[1] be true, that by means of the refractometer, the amount of albumin can be determined in a single drop of fluid, this instrument may find a welcome place in laboratories. If any other special tests are required, the urine should be divided into three equal parts and examined in small test-tubes. With less than 5 c.c. the urine must be diluted, though the results will then be less accurate.

[1] Arch. f. exp. Path. u. Pharmak., vol. 51, No. 1.

CHAPTER XI.

FUNCTIONAL EFFICIENCY OF KIDNEYS.

It is often desirable and even necessary to determine if the amount of kidney tissue present is compatible with life. In cases of nephritis with or without uremia, a prognosis may be desired, or in surgical affections of the kidney there may be indications for removing one organ. Until a few years ago the physician had as his only means such knowledge as was offered by a routine examination of the urine, notably the estimation of urea and total nitrogen present. The surgeon was often obliged to expose the supposedly healthy kidney and to determine its functionating power by such crude methods as palpation and inspection. A great advance was noted when methods came into use which permitted a separate collection of the urine from both organs. The various segregators recommended are imperfect and hardly ever employed at the present day, but in cystoscopy, by Kelly's direct method, or with one of the more complicated cystoscopes we now have a method which permits of the direct catheterization of both ureters. It is evident that much valuable information can be gained by a separate examination of both urines, but where the disease affects both organs, other methods must be resorted to.

1. Estimation of urea or of total nitrogen. The ordinary clinical methods lack accuracy, and the better methods require time and skill in chemical analysis which the practicing physician may not possess. But even if exact data are at hand, the amount of nitrogen has been found to vary within such wide limits during health, that it is impossible to draw a dividing line between sufficient and insufficient function. The character of the food plays an important part, but even with an accurate control over what is ingested, marked irregularities in the rate of excretion are sometimes observed which may be of no pathological significance. The same sources of error are present in results based upon the quantitative determination of the total salts, or what is more convenient, the total chlorides of the urine. There seems to be no constant ratio between the kidney efficiency and the quantity of chlorides excreted.

2. Determination of the amount and rate of excretion of substances injected into the blood. Formerly .05 grammes of methylene blue were injected into the gluteal musculature. After a certain time, the dye appears in the urine, partly as such, coloring the urine green, and partly as its chromogen, which is converted into the pigment by boiling the urine with acetic acid. Certain definite rules have been laid down concerning the time which elapses before the dye appears in the urine and its rate of excretion. Recent investigations, however, have shown that both are very inconstant, and that figures approximately accurate can only be given for chronic interstitial nephritis. These limitations, together with the difficulties encountered in the estimation of the amount excreted, have prevented the general application of the method. More recently F. Voelker and E. Joseph[1] claim to have discovered an ideal dye to replace methylene-blue, in indigo-carmine. Injected in doses of 16 centigrams into the gluteal muscles, it is absolutely harmless and possesses the further advantage of being excreted solely by the kidneys. The excretion is absolutely uniform; with normal kidneys it begins in fifteen to thirty minutes, reaches its maximum after two hours, and then gradually disappears during the next ten hours. An accurate study of the action of both kidneys is possible, even in cases where one cannot find the ureteral orifices, and truly beautiful pictures are obtained with the cystoscope. The method fails only in cases of prolapsed uterus and vagina, since here the discharge of urine is into a cul-de-sac behind a prominent bar of tissue and, hence, invisible to the eye. One great value of the method lies in the fact that the actual amount of functionating tissue in each kidney can be determined by observing the frequency of contraction and the size and color of the blue cloud which rises in the colorless fluid.

Phloridzine has also been injected, since this permits normal kidneys to excrete sugar. If 0.05 to 0:01 gramme is introduced subcutaneously, glycosuria will begin fifteen to thirty minutes later and last about three hours. Caspar and Richter do not pay much attention to the beginning and duration of excretion, but believe that the amount of sugar found is alone of importance. In normal cases, both sides excrete approximately the same amount, but if one kidney is diseased, considerably less sugar will be voided. Israel disputes these observations, and states that the excretion is never uniform on both sides, even in health, and that errors up to 30 per cent. still belong within physiological limits.

[1] Münch. med. Woch., Dec. 1, 1903.

3. Cryoscopy.—The principles underlying cryoscopy have already been described in Chapter II. It is impossible at this date to pass a final opinion as to the value of the method and further observations are necessary. H. Kummel and O. Rumpel[1] have resorted to cryoscopy in over 300 cases, and come to the following conclusions: With intact kidneys, the molecular concentration of the blood is a constant figure and corresponds to a freezing point of 0.56° C. In bilateral renal diseases, the molecular concentration of the blood is increased and the molecular concentration of the urine diminished, hence the freezing point of the former is lower, and of the latter higher, and more near to that of water. Unilateral renal disease does not cause general disturbance which would increase the molecular concentration of the blood. Unilateral disease can be readily detected by means of ureteral catheterization. The urine from the affected side will show diminished molecular concentration and a reduced amount of urea, while that of the healthy side will be normal. Renal diagnosis is furthermore aided by the Röentgen rays, since all stones will throw a distinct shadow.

These observations do not agree entirely with those of Israel.[2] This author states that the cryoscopy of blood gives a clear idea of renal function in a limited number of cases only, since tumors and other conditions may also change the freezing point. In nephritis, a marked hydremia may compensate for the depression, so that approximately normal figures are obtained. In discussing the phloridzine method, Israel expresses equally pessimistic views, since he does not believe that there is any relation between the sugar excreted and the amount of normal renal tissue left.

TOXICITY OF THE URINE.

Since the function of the kidneys consists in removing waste products from the organism, it is but natural to conclude that every normal urine possesses toxic properties. The first observations were brought forward by Feltz and Ritter, who made injections of unaltered urine, which were followed by the animal's death. Somewhat later, Bouchard discovered that 10-15 c.c. of urine for each kilogram of the animal will bring about intense contraction of the pupils, increased, shallow respirations and somnolency. An increased amount of urine is voided, the body-temperature falls, the

[1] Bertrag. z. klin. Chirurg., vol. 37, No. 3.

[2] Mitt a. d. Grenggebiete d. Med. u. Chirurg., vol. 11, No. 2.

reflexes are diminished and the eyeballs frequently protrude. Death soon comes on without convulsions, and sometimes the pupils dilate shortly before death. Smaller amounts cause less intense symptoms, and in about half an hour the animal may again appear normal. The amount of urine necessary to kill a kilogram of animal is termed by Bouchard a "urotoxy." The toxicity varies, however, even under normal conditions; thus, the night urine is only half as poisonous and may set up convulsions. Muscular exercise will also lower the toxicity. Many experiments have been conducted with a view of determining the poisonous principle, but these have all been unsuccessful, probably because not one but many ingredients are responsible for the symptom-complex. Thus, Bouchard speaks of seven distinct bodies, viz.: 1. An organic diuretic substance which is not destroyed by heat or removed by carbon. This is probably identical with urea. 2. An organic narcotic substance, not fixed by carbon and of unknown composition. 3. An unknown sialogogue principle. 4. An organic, convulsive substance of alkaloidal nature, especially abundant in night urine. 5. An organic substance which causes contraction of the pupils. It seems to be one of the pigments in urine. 6. A body-heat-reducing principle, which is probably also pigmentary in nature. 7. Other convulsive principles, slower in action. These are probably the salts of potassium. It seems strange that despite the most accurate analysis of urine, only two of all these substances should be known. The influence of alimentation and labor on the toxicity of urine, has been carefully studied by Casciani,[1] who finds that: 1. Persons working but little and living on a strictly vegetable diet, excrete a urine almost free from toxic properties. 2. In persons resting, urinary toxicity is greater where the individual lives on a mixed diet, and smaller with a vegetable diet. 3. A meat diet increases toxicity in direct proportion to the quantity ingested. 4. The influence of labor is greater than that of food; this is the more pronounced, the more continuous and excessive the work. 5. Excessive meat diet and excessive work cause each hypertoxicity of the urine and may produce phenomena of autointoxication.

In pathological conditions the urine may be diminished or increased in toxicity. Thus, in nephritis and uremic states, very large amounts may be injected into rabbits with impunity, while in fevers the urine may be intensely poisonous and generally shows

[1] La Riforma Medica, 1897.

more convulsive and less narcotic properties. Other conditions with very toxic urines are jaundice and liver diseases, malignant tumors, pleurisy. Various alkaloidal substances have been isolated from the urine in many of these conditions and it is a significant fact that the injected animals often present the same symptoms as the patient, especially as far as the nervous system is concerned. Various toxic principles have also been discovered in the urine of epilepsy, diabetes, Basedow's and Addison's disease.

Though the literature on the subject of urinary toxicity is very large, the practical results obtained are very small, so that this branch of urinalysis has come into disfavor and is but rarely practiced at the present day. The relations between toxicity and etiology of disease have been grossly exaggerated by Bouchard and his followers, and the presence of many of the poisonous alkaloids has not been confirmed by others. In its narrow field of usefulness the method has been replaced by other, better ones, and the physician will only rarely have occasion to inject urine into animals.

CHAPTER XII.

URINARY DIAGNOSIS.

URINE IN RENAL DISEASE.

	AMOUNT.	COLOR.	SPEC. GRAV.	ALBUMIN.	BLOOD.	SEDIMENT.	UREA AND SALTS.
Acute Nephritis.	Diminished	Pale red or dark red, turbid.	Increased.	Abundant.	Abundant.	Red and white blood cells, casts of all kinds, urates.	Urea, chlorides and phosphates reduced.
Congestion of Kidneys.	Diminished	Dark red.	Increased.	Moderate am't varying considerably.	Generally absent.	Few red blood cells, hyaline casts, urates.	Absolute amount of urea slightly diminished. Chlorides normal.
Chronic Parenchymatous Nephritis.	Somewhat diminished	Pinkish, turbid.	Normal or increased.	Abundant.	Generally present.	Red and white blood cells, casts of all kinds.	Diminished excretion of urea and salts.
Secondary Contracted Kidney.	Normal or increased.	Pale.	Slightly diminished.	Moderate.	Often a slight am't.	Many casts of all kinds.	Diminished excretion of urea and salts.
Primary Interstitial Nephritis.	Very abundant.	Pale.	Diminished	Scant.	Generally absent.	Generally only hyaline casts.	Urea and salts much reduced.
Amyloid Kidney.	Normal or increased.	Pale, yellowish.	Normal or diminished	Abundant, rarely absent	Absent.	Few hyaline and granular or waxy casts, few leucocytes.	Generally normal.

URINE IN OTHER CONDITIONS.

Fevers.—Dark, of increased acidity and specific gravity. Oliguria at first, followed by polyuria during convalescence. Urea, uric acid and sulphates increased, chlorides and phosphates diminished. Sometimes acetone is present and in very severe infections, hemoglobin or bile pigment. In typhoid, tuberculosis and measles, the diazo reaction.

Tumors.—Sometimes acetone present, and in carcinoma of the stomach, indican excessive.

Diseases of Stomach.—In an- and hypochlorhydria, indican, skatol and phenol increased. In an- hypo- and hyperchlorhydria, chlorides diminished.

Diseases of Intestines.—In obstruction of small intestines and increased intestinal putrefaction, indol, skatol and phenol increased. In ulcerative lesions, albumose sometimes present.

Diseases of Liver.—Bile if severe, or biliary passages obstructed. Urea diminished and with serious lesions (acute yellow atrophy, etc.), ammonia increased and leucin and tyrosin present.

Diabetes Mellitus.—Pale, of high specific gravity, diminished acidity and increased in amount. Urea, phosphates and ammonia increased, chlorides and other salts diminished. Glucose and sometimes other sugars present, in severe cases, acetone, diacetic, β-oxybutyric and a-crotonic acids. Urine may possess property of dissolving gentian violet.

Diabetes Insipidus.—Pale, low specific gravity, increased amount. Urea, chlorides and other salts diminished.

Gout.—Acidity increased, uric acid and xanthin bases increased or diminished.

Leucemia.—Uric acid and xanthin bases increased.

Suppurations.—Indican increased, albumin present, chlorides often diminished.

Bone Tumors (especially multiple myelomata).—Sometimes Bence-Jones bodies.

Cystitis.—Urine faintly acid or alkaline, contains mucus, pus cells and bacteria.

Pyelitis.—Urine generally acid, contains less pus than in cystitis, and may show caudate cells.

Suppurative Nephritis.—Urine may contain pus, pus casts and sometimes bacterial and other casts.

CHAPTER XIII.

REAGENTS NECESSARY FOR URINALYSIS.

A.

Acetic acid mixture (phosphates)
- Sod. acetate, 100
- Acid acetic, 30
- Water to make 1000

Acid acetic glacial, 50%, 10% and 2%.
Acid betanaphthol sulphonic
Acid hydrochloric
Acid indigotin disulphonic
Acid metaphosphoric
Acid nitric c.p.
Acid nitric, fuming
Acid nitrous-sulphuric (uric acid)
- Acid sulphuric c.p. 25 c.c.
- Acid nitric, fuming, 1 c.c.
- Water, 75 c.c.

Acid orthonitrophenyl propiolic
Acid paradiazo benzolsulphonic
Acid picric
Acid phosphomolybdic, 10%
Acid phosphoric
Acid phosphotungstic, 10%
Acid rosolic 1% alcoholic solution
Acid sulphosalicylic, substance and 12.5 % solution
Acid sulphuric, concentrated and 5%
$\frac{n}{1}$=48.91 gme to litre
$\frac{n}{2}$=24.46 gme to litre
$\frac{n}{10}$ 4.89 gme to litre
Acid tannic
Acid trichloracetic
Albumin
Alcohol, 95% and absolute
Alcohol amylic
Alizarin
Ammonia water
Ammonia-ferric alum (sat. solution)
Ammonia-carb.
- chlor.
- molybd.
- oxalate
- sulphate, cryst. and sat. sol.

B.

Barium chloride, sat. sol.
Barium hydrate
Barium mixture
- Barium chloride, 10
- Caustic baryta, 3-4

Benzoyl chloride
Bial's reagent (pentose)
- Orcin, 0.5
- liq. feri sesquicklor, 10 drops
- Acid muriat. conc., 250.0

Bismark brown, 1% aq. solution
Bromine water
Brücke's reagent (sugar)
- 1.5 gme. fresh bism. subnitr. heated to boiling with 20 c.c. water. Add 7.0 gme. potass. iodide and 1.5 gme. hydrochloric acid

C.

Calc. carbonate
Calc. chloride
Calc. oxalate (1-1000)
Cane sugar
Carbol. gentian. violet
- sat. alc. sol. gent. violet, 10
- 5% carbolic acid, 90

Carbon disulphide
Charcoal
Chloroform
Copper spiral
Copper sulphate, 1% and 10%

D.

Dimethyl amidobenzaldehyde, 2% solution

E.

Echt-gelb, 1% aqueous solution
Ehrlich's solution (diazo)
- (a) Acid sulfanilic, 1
  Acid hydrochloric, 5
  Water to make 100
- (b) Sod. nitrite, 0.5
  Water to make 100

Esbach's solution (albumin)
- Acid picric, 10
- Acid citric, 20
- Water, 1000

Ether

F.

Fehling's solution (sugar)
- (a) Copper sulphate, 34.369
  Water, 500
- (b) Rochelle salts, 173
  Caustic potash, 125
  Water, 500

Fibrin
Fuller's earth

G.

Glycerine
Gram's solution (bile)
  Iodine, 1
  Potass. iod, 2
  Water, 300
Gunning's solution (nitrogen)
  Acid sulphuric conc., 15
  Potass. sulphate, 10
  Copper sulphate, 0.5

H.

Hydroxylamine hydrochlorate

I.

Iodine, crystals and $^{n}/_{10}$ solution = 112.653 gme. to litre
Iron chloride, substance and official solution
Iron sulphide

J.

Jenner's stain (eosinate of methylene blue)
Jolles' reagent (albumin)
  Merc. bichlor, 10
  Acid succinic, 20
  Sod. chloride, 10
  Water, 500
Jolles' reagent (bile)
  (a) Iodine, 0.63
    Alcohol, 125
  (b) Merc. bichlor, 0.75
    Alcohol, 125
  Mix (a)+(b) and add 250 pure hydrochloric acid

L.

Lead, acetate, substance and conc. solution
Lead foil
Lime, chloride of
Lime, milk of
Liq. plumbi subacet.
Lugol's solution, see Gram's solution

M.

Magnesia, milk of
  Magnes. ust, 1
  Water, 12
Magnesia mixture (xanthin)
  Magnes. sulphate, 1
  Ammon. chloride, 2
  Aq. ammonia, 4
  Water, 8
Magnes. sulphate, sat. sol.
Magnes. usta
Magnes. wire
Maschke's reagent (sugar)
  Sod. tungstate, 30
  30% acetic acid, 75
  Aq. dist. water, 120
Methyl orange
Mercury bichloride, 10% and sat. solution
Mercury oxide, freshly precipitated
Methylene blue
Millon's reagent (phenol)
  Mercury, 1
  Fuming nitric acid, 1
  Water, 2

N.

Napthol
Neutral-red, sat. aqueous sol.
Nylander's solution (sugar)
  Bism. subnitr, 2
  Rochelle salts, 4
  Sodium hydrate, 10
  Water, 90 (boiled and filtered)

O.

Obermayer's reagent (indican)
  2—1000 solution of iron sesquichloride in concentrated hydrochloric acid
Oil of turpentine (ozonized)

P.

Pancreatin
Pappenheim's solution (staining)
  Fuchsine, 1
  5 % acid carbolic, 100
  Absol. alcohol, 10
Para-amido-aceto-phenon
Phenol phthaleine, 1% alc. sol.
Phenylhydrazine hydrochlorate
Phenylhydrazine oxalate
Phloroglucin
Platinum foil
Potass. carb.
Potass. chrom., 10% sol.
Potass. ferrocyanide, 10% sol.
Potass. iodide, $^{n}/_{50}$ sol.
  3.32 gme. to 1 litre
Potass. nitrate
Potass. permang., $^{n}/_{20}$=1.576 to 1 litre
  Crystals and 0.30 %
Potass. platinocyanide
Potass. sulphocyanide $^{n}/_{50}$ sol. = 1.939 gme. to 1 litre. For chlorides = 6.6 to 1 litre
Pyridine

R.

Resorcin
Rudisch's solution (sugar)
  Copper sulphate, 4.78
  Sodium sulphate, 50
  Sodium carb. cryst., 80
  10% ammonia ad., 500
Ruhemann's solution (uric acid)
  Iodine, 1.5
  Potass. iodide, 1.5
  Absol. alc., 15
  Water, 185

S.

Silver nitrate, 10%; 30% $^{n}/_{10}$= 16.955 gme. to 1 litre. $^{n}/_{50}$ (Rudisch) = 3.3932 silver nitr., 75. aq. ammonia sp. gr. 0.9, 10.0 am. chloride, water to make 1000.
  for chlorides = 29.059 gme. to litre
Sod. acetate (sat. sol.)
Sod. bicarbonate
Sod. carbonate
Sod. chloride (sat. sol.)
Sodium hydrate sp. gr. 1.16 and 1.34
  $^{n}/_{1}$ sol.=39.96 to litre
  $^{n}/_{2}$ sol.=19.98 to litre
  $^{n}/_{4}$ sol.= 9.99 to litre
  $^{n}/_{10}$ sol.= 3.996 to litre
Sodium hypobromite solution (urea)
  Bromine, 5 c.c.
  30% by volume sod. hydrate, 70 c.c.
  Water, 180 c.c.
Soda lime
Sodium nitrite, 1% solution
Sodium nitroprusside, 5% sol.
Sodium throsulphate
  $^{n}/_{1}$ sol.=24.764 gme. to litre
  $^{n}/_{10}$ sol.= 2.4764 gme. to litre
Sodium tungstate
Spiegler's reagent (albumin)
  Merc. bichlor, 8
  Acid tartaric, 4
  Glycerine, 20
  Distilled water, 200
Spirits of ammonia, 10%
Starch

T.

Talcum
Thymol
Tinct. Guaiac

U.

Uran. acetate
Uran. nitrate, 44.78 to litre

X.

Xylidin

Y.

Yeast

Z.

Ziehl's solution (staining)
  Sat. alc. sol. fuchsine, 10
  5% carbolic acid, 90
Zinc c.p.
Zinc acetate, 10% sol. in abs. alc.
Zinc chloride alc. solution, spec. grav. 1.20

THE FECES.

CHAPTER XIV.

MACROSCOPIC EXAMINATION OF THE FECES.

Frequency.—The "normal" frequency of defecation is as little capable of exact definition as is the amount, depending, as it does, both on idiosyncrasy and a number of other variable factors. The amount of fecal residue, its character, whether irritant to the motor functions of the gut, or not, and, reciprocally, the condition of neuro-muscular mechanism of the lower extremity of the intestinal canal, all play an important rôle. It is highly probable that the inflammatory exudations of intestinal disease, together with the products of the bacterial agents, exercise a markedly irritant effect, with the production of frequent stools. On the other hand, psychical, general nervous, and reflex nervous impulses are also important elements. The diarrhea of fear, and of such diseases as Basedow's, are an example of the former, while it is well known to what an extent even slight local lesions of the rectum, such as an ulcer or a fissure, may impose as irritative diarrheas. Constipation, likewise, may be due to a variety of lesions in the neuro-muscular apparatus. For example, to tabes, melancholia, lesions of the cord, or atony of the musculature. These are all conditions which may produce symptomatic disturbances of the defecating function, which may be of enormous import for the life and health of the patient.

It has been stated that at the one extreme two stools daily, and one stool every forty-eight hours, at the other, may be regarded as the normal limits, but this statement is very arbitrary, and it is certainly wiser to take the general condition of the patient as a guide to the sufficiency of defecation. Certain individuals would suffer from copremia under conditions which to others are highly satisfactory.

rarely possible to determine, inasmuch as the two functions generally suffer simultaneously and contribute alike to the end-result; as for example in amyloidosis or tabes mesaraica (tuberculosis of the mesenteric and retroperitoneal lymph nodes). The pathological contribution of the gut may take the form of pus, mucus, blood, fibrin, or a combination of these, and may at times add quite considerably to the amount of the fecal matter.

The diagnostic application of these data is unfortunately not as yet very far advanced; nevertheless the way has been definitely pointed to their value in medicine. Schmidt, for example, has definitely shown that the fecal matter thrown out after the use of his "test-diet" is far greater in case of fermentative dyspepsias than under normal conditions. Furthermore, in case of bottle infants, observation of the amount of the various fecal constituents gives valuable hints regarding the regulation of the diet.

Amount of Fecal Matter.—The total amount of fecal matter which is passed within twenty-four hours may vary enormously. It depends entirely, other factors being equal, on the degree of preceding activity of the bowels. Thus Lynch has recorded a record stool of 20 kilos after an enema.

The chief factors which determine the amount of feces are: 1. Quantity and quality of the food. 2. Quantity of digestive juices, etc. 3. Condition of the digestive organs.

1. *Quantity and Quality of the Food.*—As has been previously stated, foods may be distinguished as digestible and as largely indigestible. The latter leave a large fecal residue, and also stimulate a more active secretion of the intestinal juices, and tend to increase the amount of fecal matter, while, in case of the former, the tendency is just the reverse. With a given form of diet, similarly, the amount of fecal matter will necessarily increase with an increase in the amount taken per ounce.

In a series of observations made on healthy individuals of varying ages by different investigators the following results were obtained:

	Age	Food	Amount of feces grammes
1.	Child of one month	Breast milk	3.3
2.	(a) Child of two months	" "	6.5
2.	(b) Child of three months	Cow's milk	51.6
3.	Child of seven months	Varying diets	15.56
4.	Child of nine months	Cow's milk, with additions	5.9
5.	Child of ¾ to two years	Mixed	77.0
6.	Child of four years	"	101.0
7.	Child of six years	"	134.5
8.	Child of nine years	"	117.0
9.	Child of eleven years	"	128.0
10.	Adults	"	131.0

In experiments made by Rubner, it was found that the same individual under normal conditions yielded 95 grammes fresh feces in the twenty-four hours on a diet of 689 grammes of bread; and 109 grammes per day, on a diet of 1,237 grammes.

As a general rule, it is found that pro kilo of body-weight adults form far less fecal matter daily than do the young, as is shown by the following table taken from Camerer:

Year	Feces Grammes	Amount of feces: Pro. 1 kilo milk Grammes	Amount of feces: Pro. 1 kilo body weight Grammes
1. Five months	56	35.2	**8.3**
2. Eight years	112	51.7	6.3
3. Sixty-six years	60.4	29.0	0.0

The form of diet has enormous influence on the quantity of fecal matter. Thus, in a table of Biedert's, the feces in children fed on—

a. Breast milk	The feces, in percentages of the dry residue of food, amounted to	1.0—1.3 %
b. Artificial diet		2.0—3.1 %
c. Very variegated diet		5.9—7.5 %

A similar basis of reckoning underlies the following table:

Diet	Amount	Amount of feces in grammes: Fresh	Dry residue	Per cent. of dry residue
1—Mixed	——	131.0	34.0	25.9
2—Vegetable	——	370.6	——	——
3—Milk	3075	174.0	40.6	23.0
4—Milk and Cheese	2050 and 218	88.0	27.4	31.1
5—Eggs	948	64.0	13.0	20.3
6—Meat	1435	64.0	17.2	26.9
7—White Bread	1237	109.0	28.9	26.5
8—Rice	638	195.0	27.2	13.9
9—Macaroni	695	98.0	27.0	27.5
10—Maize	750	198,0	49.3	24.9
11—Potatoes	3078	635.0	93.8	14.7
12—Brown Bread	1360	815.0	115.8	14.2
13—Peas	9598	927.1	124.0	13.4
14—Carrots	5133	1092.0	85.0	7.7
15—Cabbage	3831	1670.0	73.8	4.4

It is evident, therefore, that the form of diet influences the quantity of fecal matter to an enormous extent; those elements which contain a very small indigestible residue (meat, eggs, cheese, white bread, etc.) give a fecal residue which falls below the normal average, while this is exceeded again in diets rich in cellulose.

2. *Quantity of Material Contributed by the Intestinal Tract.*— This is the second factor of importance. It is an extremely diffi-

cult matter to estimate this factor with anything approaching to accuracy. The feces of fasting individuals represent, of course, simply and solely this element, but the same calculation cannot be transferred to the feces of individuals on a regular diet. During starvation, various calculations have yielded from 2-6 grammes of dried residue of the feces passed within twenty-four hours. Schmidt and Strasburger estimate that on an animal diet, free from indigestible residue, the dry residue of the daily feces amounts to 13-17 grammes, of which the major part is contributed by the intestinal tract and by the bacteria.

3. *Condition of the Digestive Organs.*—It has already been pointed out that deficiency in the digestive juices, by failure properly to act upon the food, may increase the daily amount of feces. The same holds true of anomalous conditions of peristalsis and of absorption. Pathological conditions associated with the excretion of large masses of pus, mucus, etc., notably alter the amount of fecal matter.

Form and Consistence.—The consistency of the fecal mass is chiefly determined by the amount of water which it contains. This is not invariably the case, inasmuch as certain forms of thin, or gruel-like, stools owe their softness not to water, but to an abnormal amount of fats, mucus or swollen vegetable constituents. Microscopical examination, or even, as a rule, careful inspection, suffices to differentiate these conditions. An increase of fluid in the stools may be due either to exudation or transudation from the mucous membrane, or to deficient absorption. It is extremely important, but not always easy, to differentiate between these conditions. If the fluid stool contain other evidences of inflammation, such as pus, mucus or blood, it is fair to regard the fluid as part of the exudate. The absence of these accompaniments does not, however, exclude an exudative origin, inasmuch as they may have undergone digestion. In this case one thinks either of transudate or of deficient absorption. If the fluid stools contain many epithelia, especially in shreds or flakes as in cholera, the probability is strong that there has been transudation through the denuded wall of the gut. On the other hand, the presence of large amounts of undigested food particles, especially fat or muscle, argues for absorptive disturbances, not necessarily, however, for organic disease. Thus, increased peristalsis for any cause, whether nervous or due to the nature of the diet, suffices to produce a watery stool through failure of absorption. In the absence of colic, how-

ever, and of inflammatory products, a watery stool rich in undigested food elements argues for organic disease, notably amyloidosis or tabes mesaraica.

Delayed peristalsis, with a prolonged sojourn in the colon and rectum, lead to excessive absorption of water, with the formation of an extremely hard fecal mass. Normally the stool is conical and of a certain medium, uniform caliber. In constipation, however, it is apt to become considerably larger and irregular through the presence of numerous knob-like protuberances which represent the intestinal haustra. The term scybalæ is often used to denote the small and extremely hard, often dark, fecal masses which occur in constipation from any cause. It is probable that their formation is due to a prolonged sojourn of the feces in the recesses of the wall of the colon.

Much importance was formerly attached to the "lead pencil" stools as affording evidence of a stricture low down in the gut, and a similar significance was attached to the "sheep stools." It is now known, however, that these conditions may exist entirely independent one of another, so that in this particular the evidence of the stools must be disregarded. Spastic conditions of the gut may often be recognized by the small caliber of the stool, on which are to be seen the longitudinal markings of the muscular tæniæ of the colon.

Color of Stools.—The color of the stools affords diagnostic information of very great importance, but is, unfortunately, somewhat difficult at times to interpret. The normal color in adults is a dark brown, which is contributed by the oxidation products of the bile pigments. The variations in color, due to the food constituents, may considerably alter this tone, however. Thus, a predominantly meat diet gives a stool which is intensely brown, owing to the reduction of the hemoglobin. This shade becomes almost blackish after the use of a dish much in use among the German element of the population and known as "Blutwurst." A vegetable diet gives a more yellowish shade to the feces. The presence of undigested fats, as due pathologically to the failure of the bile to enter the gut, imparts a yellowish or even whitish tint. Other discolorations due to occasional or accidental admixture of special foods or drugs will be subsequently mentioned.

Conner[1] has contributed recently to this important topic, and has suggested a provisional classification which is helpful. He finds it convenient to group the color changes as influenced by four

[1] Medical News, Aug. 30, 1902.

main series of features. These are: 1. Digestive secretions. 2. Food residue. 3. Discharges from the intestinal mucous membrane. 4. Accidental ingredients, *e. g.*, drugs, etc.

1. *Digestive Secretions.*—These secretions take a considerable part in the making up of the fecal mass. This is evident from the fact that in conditions of starvation or fasting, when the intestines contain no food whatever, the feces, which then consist only of the digestive secretions, mucus, desquamated epithelium and bacteria, are of considerable quantity and of dark, pitch-like appearance.[1]

Of the various digestive juices the bile is the chief one taking any considerable part in furnishing color to the stools. Its rôle is an important one, however, and the history of the changes of this coloring matter from the time of its formation in the liver to its exit at the anus is instructive.

The bile as secreted contains a single pigment—bilirubin. A part of this bilirubin is promptly oxidized, either in the bile passages or soon after reaching the intestines, into biliverdin and several allied bodies. In meconium and in the stools of nursing infants, where putrefactive changes are slight or absent, biliverdin and bilirubin respectively appear as the normal ingredient. After the first few months of life, however, the bile pigments, under the influence of the putrefactive bacteria in the intestine and other enzyme actions, undergo a process of reduction to hydro-bilirubin and intermediate products, and thenceforth never appear as constituents of normal stools. This hydro-bilirubin then, a reduction product of bilirubin, constitutes the normal yellowish-brown pigment of the feces. It was described in 1871 by Vanlair and Masius,[2] who called it stercobilin. Soon afterward this was shown by Maly[3] to be identical with the urinary pigment urobilin. The change from bilirubin takes place usually in the small intestine, and both Frerichs and Nothnagel[4] have demonstrated by post-mortem examination that under normal conditions, neither bilirubin nor biliverdin, as shown by their positive reaction to Gmelin's test, are found in the contents of the intestine below the cecum. A certain amount of hydro-bilirubin frequently, and perhaps always, undergoes still further reduction to a colorless body called by von Nencki leuco-urobilin. It is to the presence of this

[1] Fr. Müller, Zeitschrift für Biologie, XX, 1884, p. 327.
[2] Centralblatt für med. Wissenschaften, IX, 1871, p. 369.
[3] Centralblatt für med. Wissenschaften, IX, 1871, p. 849.
[4] Die Erkrankungen des Darms, etc. (Spec. Path. u. Ther. Bd. XVII), Wien, 1898, p. 9.

colorless chromogenic body and its gradual oxidation back to hydro-bilirubin that Quincke[5] ascribes the gradual darkening in color which the surface of feces undergoes upon exposure to the air. This darkening in color upon exposure to the air is explained by Fleischer[6] as due simply to a process of drying and not to any chemical change, and he explains in the same way the very dark color of feces which have remained for a long time in the rectum.

It follows from what has been said that variations in the color of the stool may permit of very important conclusions as to the condition of the liver and bile passages. If the stools are free from bile pigmentation they exhibit a pale color, the well-known "clay-colored" stools of biliary obstruction, the color of which is, however, also partly attributable to the presence of large amounts of undigested fats. An important diagnostic point is the recognition of certain pseudo-acholic stools which present a similar shade in the absence both of icterus of the skin and of any disturbance in fat digestion. They are due to the further reduction of bilirubin to colorless leuco-urobilin and become considerably darker on exposure to the air through reoxidation of the pigment. If calomel be given to such individuals the stools regain their normal color, owing to the fact that the drug restrains the decomposition processes which free certain powerful reducing agents.

In many diarrheas the stools present the golden yellow color of bilirubin, instead of the urobilin tint, owing to the fact that the stool is so rapidly carried through that there is not sufficient time for the processes of reduction to be completed.

In the stools of infants the bile pigments occur normally in the unreduced form, as bilirubin, which gives them their golden yellow tint. Chemically, the presence of this bilirubin is easily determined by Gmelin's reaction. Admixed with the bilirubin in the stools of infants is a certain amount of biliverdin. It is of importance, however, to note that the green stools of infant diarrheas are frequently due to the action of a pigment producing bacillus (not the common *Bacillus pyocyaneus.)*

An alkaline reaction in the intestinal content is essential to this series of changes. This fact explains the absence of the reduction products in certain acid diarrheas, *e. g.*, in typhoid.

Under certain circumstances, to be spoken of later, most or all of the hydro-bilirubin may be reduced to leuco-urobilin and then the stools may simulate the clay-colored feces of jaundice.

[5] Münch. med. Woch., 1896, p. 854.

[6] Lehrbuch der inneren Medicin, Wiesbaden, 1896, p. 1161, *et seq.*

But the bile derivatives are not the only coloring matters supplied by the digestive secretions. Ehrenthal[7] found that in starving dogs with biliary fistulæ—*i. e.*, dogs in which neither food nor bile entered the intestine—dark-colored, pitch-like feces were passed whose color he ascribed to the pancreatic juice. Under normal conditions, however, this secretion probably has little influence in determining the color of the stools.

2. *Food Residue.*—With the usual mixed diet the food residue plays only a subordinate part in the make-up of the fecal color, but where the food has a pronounced and distinctive color this may modify considerably the appearance of the feces. So, for example, vegetables rich in chlorophyll, such as spinach or lettuce, may give a greenish tint to the dejections and the abundant ingestion of carrots is said sometimes to impart their distinctive color.[8]

In general a vegetable diet produces much lighter colored stools than does a diet chiefly of meat. A meat diet alone is associated with very dark brown feces in which the color is due in part to the conversion of the blood-coloring matter of the meat into hematin (Fleischer). A diet of milk produces the familiar yellow or yellowish-white stools.

In infants fed upon breast milk the feces have the orange yellow color of the yolk of egg; the color being due to the presence of unchanged bilirubin, which, owing to the absence of putrefactive processes, is not changed in the intestine. With babies fed upon cow's milk, however, the stools have regularly a lighter, yellowish-white color.

By the action of the alkaline contents of the intestine the red coloring matter of certain fruits, such as blackberries and huckleberries, is so changed as to give to the stools a dark brown or slightly greenish hue. Red wine is said to produce a somewhat similar color.

Quincke has called attention to the fact that the degree of translucency of the ingredients of the feces has some effect upon the color; that with the same quantity of coloring matter the stools appear the lighter the more they contain of such highly refractive bodies as fat droplets, crystals and gas bubbles.

3. *Discharges from the Intestinal Wall.*—Among those which may modify the color of the dejections are mucus, pus, serum and blood.

Mucus, although so common a constituent of pathological stools,

[7] Arch. f. d. ges. Physiologie, XLVIII, 1891, p. 74.
[8] Schmidt u. Strasburger. Die Feces des Menschen, Berlin, 1901, p. 21.

does not usually give to them a distinctive color. When in large quantities, however, and when thoroughly mixed with the feces these have a glistening, grayish or yellowish-gray appearance.

Pus will, in rare instances, give a distinct yellowish or yellowish-gray tone to fluid stools. That this may occur two conditions are necessary; first, that the pus be in large amount and, second, that it come from the lower part of the large intestine, since pus originating higher in the intestine is so rapidly changed as to be unrecognizable in the stools by the naked eye. It is rarely seen, therefore, in the stools except as the result of the rupture of some perirectal abscess.

Serum, aside from giving to feces a watery consistence, will also impart its own straw color when the usual fecal pigment is lacking as, for example, in the rice-water stools of cholera, in which there is usually cessation of the biliary secretion.

Blood can give to the feces a great variety of tints, depending upon its amount and upon the degree of change which it has undergone. This latter corresponds usually to the length of time which the blood has remained in the intestine; so that, in general, blood from the rectum or sigmoid flexure, which is promptly discharged, retains its normal color, whereas blood from the small intestine will have undergone such change, by the conversion of its hemoglobin into hematin, that it presents an appearance suggestive of coffee grounds or of tar. In such instances Teichmann's test for blood is useful in the determination. The presence of iron confuses the picture somewhat, as this remedy is often given after hemorrhage, and thus may constitute a source of error. Quincke has said, however, that the stools containing iron change their color to a blackish shade only after being exposed for some time to the air, while the stools of melena are passed in their tarry condition.

The appearance of the blood indicates the location of the bleeding, however, only in a very general way, since with especially active peristalsis blood from high up in the small intestine may be discharged so promptly that little change will have occurred. If the blood be in small quantity and be intimately mixed with the feces it may give to the stools an orange tint suggestive of paprika (Nothnagel[9]). Finally, it must be remembered that certain articles of diet, *e. g.,* cocoa, huckleberries, etc., may produce in the stools an appearance which may easily be mistaken for disorganized blood.

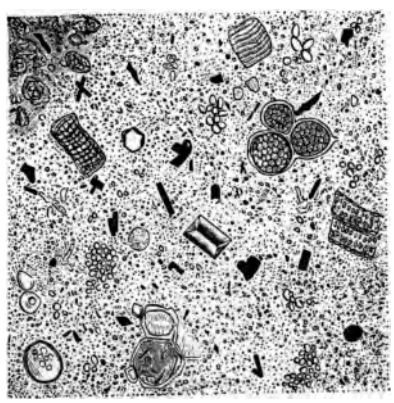
[9] Die Erkrankungen des Darms, etc., p. 84.

4. *Accidental Ingredients.—Drugs.* Among the most interesting of the variations in the color of the stools are those produced by the use of certain drugs; and concerning certain of these changes there is much popular misapprehension.

Bismuth preparations produce a blackish or dark green color by the reduction of the ordinary salts (sub-nitrate, sub-carbonate, etc.) to bismuth hydroxide, and not the bismuth sulphide as so commonly believed (Quincke).

Calomel, contrary to the general impression, causes greenish stools (in adults at least) only infrequently and then, Quincke believes, not by the formation of sulphide of mercury but, apparently, by checking the putrefactive processes and by so preventing

FIG. 66.



Sulphide of bismuth crystals in the feces. (v. Jaksch.)

the reduction of all the bilirubin; so that instead of hydro-bilirubin the feces contain the greenish biliverdin.

Iron usually does not affect the color of the stools until they have been exposed to the air for some time, when they become blackish gray, not from the presence of iron sulphide, but by the oxidation of some organic compounds of iron (Quincke.)

Rhubarb, Senna and *Santonin* are said sometimes to give to the feces a yellow color.

Methylene Blue causes no discoloration of the stools as passed, but within a few minutes these take on a bluish-green tint which gradually deepens.

Kino colors the stools bright red, and *Hematoxylin* imparts a violet to violet red coloration.

In this connection it is well to emphasize the fact that many stools, both those of infants and of adults, change their color very materially upon exposure to the air. Under such circumstances it is important to compare the color of the interior of the fecal mass with that of the surface.

Bacteria.—In certain of the green diarrheas of children, Lesage[10] has found a bacillus, not *Bacillus pyocyaneus,* which develops in cultures a green pigment and which, he believes, stands in casual relation to the diarrheas.

Salus[11] asserts also that *Bacillus pyocyaneus* can under certain circumstances give a greenish color to the stools. The common water *Bacillus fluorescens* and its congeners may induce a light fluorescence in the feces of infants.

Clay-Colored Stools.—The association of grayish-white or "clay-colored" feces with obstructive jaundice has long been noticed and their lack of color, very naturally, ascribed to the absence of the bile coloring matters. Some years ago, however, Bunge[12] announced that these acholic stools owed their clay color not to the absence of bile, but rather to the presence of an excessive quantity of fat, and he showed that by extracting this fat with ether such stools assumed a much darker color, which color he attributed to the presence of hematin and sulphide of iron from the food.

The fact that the feces in obstructive jaundice contained enormous quantities of minute needle-shaped crystals had been noticed before. Gerhardt[13] believed these to be crystals of cholesterin. Their true nature as fat crystals had been proved, however, by Oesterlein,[14] Stadelmann,[15] and others. Franz Müller[16] in some very careful investigations showed that, whereas in normal feces only from 7 to 10 per cent. of the ingested fat could be recovered, in obstructive jaundice the feces contained from 55 to 78 per cent. of the total quantity of fat eaten. That the gray color of such stools was due, however, to this fat and not to the lack of bile remained for Bunge to show. His observations were soon verified by Fleischer.

Clay-colored feces, in cases of jaundice, in which neither bilirubin nor hydro-bilirubin could be found, would invariably, upon

[10] Archives de Physiologie, IV, Série, Tome I, 1888, p. 212.
[11] Prag. med. Woch., 1894, No. 33.
[12] Lehrbuch d. physiol. u. pathol. Chemie, Leipzig, 1887, p. 192.
[13] Zeitschrift für klin. Med., Bd. VI, 1883.
[14] Mittheilungen aus d. med. Klinik in Würzburg, Bd. I, 1885, p. 1.
[15] Deutsch. Arch. für klin. Med., Bd. XL, 1887, p. 372.
[16] Zeitschrift für klin. Med., XII, 1887, p. 101.

treatment with ether, thus extracting the fat, show a much darker color. Fleischer was unable, however, to demonstrate iron sulphide in such stools and believes the color to be due to hematin alone. But Ehrenthal has shown that the bile is not the only digestive secretion which gives color to the feces, and it seems probable, therefore, that this resulting color may depend upon several causes.

Colorless Stools Without Jaundice.—It has also been noticed for a long time that typical, gray, clay-colored feces are occasionally to be seen where there is neither jaundice nor other evidence of biliary obstruction. Such stools have been seen by Nothnagel[17] in leucemia, in cancer of the stomach and the intestines, in intestinal catarrh in children, and especially in cases of advanced phthisis. Von Jaksch[18] has noticed them in intestinal tuberculosis, chronic nephritis, chlorosis and scarlatina. Berggrün and Katz[19] have called attention to their great frequency and their diagnostic value in chronic tuberculous peritonitis in children.

Such light-colored stools seem, as regards their causation, to fall into two fairly distinct classes. 1. Those in which the lack of color is due to the great amount of fat present. 2. Those in which most of the bilirubin has been reduced beyond the stage of hydrobilirubin to the colorless body leuco-urobilin (leuco-hydrobilirubin).

An excess of fat in the feces may result from several causes other than the lack of bile. (*a*) Ingestion of an unusually large quantity of fat even with normal digestion. (*b*) Disturbances of the fat absorption in the small intestine; as, for example, with atrophy, amyloid degeneration, or tuberculosis of the mucous membrane, and especially by the occlusion of many lymph channels such as occurs with caseation of the mesenteric lymph nodes in *tabes mesenterica* and in chronic tuberculous peritonitis. Berggrün and Katz have shown that the light-colored stools so frequently seen in chronic tuberculous peritonitis in children depend upon an excessive amount of fat, and they regard such stools as of considerable diagnostic significance, since the presence in them of hydro-bilirubin is proof that the fat is not due to the absence of bile. (*c*) Finally, it is possible that the absence of the pancreatic juice from the intestine may occasionally cause such fat stools. That it always, or even usually, does so, however, is certainly not

[17] Die Erkrankungen des Darms, etc., p. 18.

[18] Klin. Diagnostik inneren Medicin, II Auf., Wien, 1889, p. 213.

[19] Wien. klin. Woch., 1891, p. 858.

the case. Much of the clinical evidence is entirely opposed to the view that disturbed pancreatic function is associated with an increased amount of fat in the feces (Nothnagel).

Of the second class of clay-colored stools without jaundice—those due to the reduction of bile pigment to the colorless body leuco-urobilin—much less is known. It is certain that not all such stools contain an excess of fat. Quincke states that this reduction to leuco-urobilin may be so great that for weeks at a time, without obstruction to the bile, almost colorless feces may be discharged in which the extraction by alcohol furnishes an abundance of hydro-bilirubin. The conditions favoring this abnormal reduction of bile pigment to leuco-urobilin are by no means clearly understood. They seem to be connected usually, however, with increased putrefactive changes in the intestines.

The separation of these two types of colorless stools is usually not difficult, since the second class can be identified by the lack of an increased quantity of fat and by the prompt darkening of color, upon treatment with acid alcohol, as the leuco-urobilin is oxidized to hydro-bilirubin.

Green Stools.—These, except in those infrequent cases in which the color is due to definite chromogenic or fluorescent bacteria, or to the food, are always caused by the presence of biliverdin. This pigment may be said never to occur as a normal constituent of the feces except in meconium. In infants, however, where the putrefactive processes in the intestines are slight, and where bilirubin is found normally in the feces, biliverdin will appear upon slight provocation. The green color may be present when the stool is passed or may develop only after it has stood for some time.

Biliverdin is found in the stools of children in diarrheas of many sorts. Such stools are usually alkaline in reaction, and both Pfeiffer[20] and Biedert believe that the appearance of biliverdin is associated with increased alkaline reaction of the contents of the upper part of the small intestine.

In adults green stools are of much less frequent occurrence, but are occasionally seen in certain diarrheas. Fleischer believes that they occur only where there is inflammation with increased peristalsis of *both* small and large intestine and never when one or the other alone is involved, since with normal peristalsis in either large or small intestine there would be time for the reduction of the biliverdin to hydro-bilirubin.

Odor.—The odor of the stools in starvation is practically nil.

[20] Jahrbuch für Kinderheilkunde, XXVIII, 1888, p. 164.

It is the fermentation and putrefaction of the food which lends the stool a characteristic and often diagnostic odor. The odor of normal adult stool is chiefly derived from the products of proteid decomposition, indol, skatol, etc., and is, therefore, stronger in case of predominantly meat diet, in constipation, and in certain forms of putrefactive dyspepsias due chiefly to bacteria. The excessive decomposition of carbohydrates gives an odor of acetic or butyric acid. The latter fact affords an important sign in case of infant dyspepsias, inasmuch as the normal stool of infants has practically no odor. The stools in many forms of diarrheas, *e. g.*, cholera, dysentery, are so rapidly passed and voided that there is no time for decomposition, hence no odor. In amebic dysentery the stools have a peculiar, glue-like odor. The stools of dysentery and intestinal carcinoma have often a very sickening, stinking odor.

Macroscopic Elements.—The elements macroscopically recognizable in the feces are derived either from the food or from the intestinal apparatus itself. As regards the remains of the food, it has long been known that these are recognizable as such, and the older authors were accustomed to describe as characteristic of "lientery," a stool in which large amounts of undigested materials were present. Unfortunately this fairly accessible branch of coprology is not at present of great diagnostic moment.

Food remains may occur in the feces because they are essentially indigestible. In this category belong masses of cellulose, bone, epidermis, the skin of many fruits, etc. Again, insufficient subdivision of the particles, or imperfect cooking, may be responsible for the passage of food boluses, notwithstanding a normal condition of the digestive tract. Similarly, if a considerable excess of any particular article of diet be present in the food a certain amount of this may be rejected and reappear in the feces unaltered. Aside from these examples, however, the presence of masses of undigested articles may be regarded as indicative of disease. A special interest attaches to the occurrence of fish bones and of animal connective tissue, inasmuch as these are digested solely in the stomach and may be interpreted as evidence of gastric inefficiency. In every other particular, however, the gastric digestive functions are replaceable by those of the intestine, and even complete achylia gastrica does not otherwise affect the character of the stools. Starchy foods are the most easily digested element in the normal diet, and do not appear in the feces except when ensheated by a layer of cellulose, or in cases of increased peristalsis with diarrhea. Meats when properly prepared are also easily digestible,

and their presence in the feces argues a serious fault in digestion. This may be due either to absence of the pancreatic secretion, as in cases of blockage of the duct or of atrophy of the gland, or to absence of the succus entericus, which contains the recently discovered ferment "enterokinase," (Pavlow) as in cases of amyloidosis and of tabes mesaraica. Not only secretory disturbances, however, but rapid propulsion of the food through the gut, as in cases of diarrhea, may produce the same phenomenon of undigested muscle in the stool. Thus, its presence cannot be regarded as pathognomonic of any particular condition, but must be brought into relation with other phenomena.

The presence of another proteid, casein, in the stools of infants is easily recognizable by the whitish, crumbly appearance, and is of considerable diagnostic value. Fats rarely appear in recognizable amount in the feces. In cases of biliary obstruction, however, they are undigested, and may appear either finally divided throughout the feces, in which case they are recognizable by the whitish color, or, more rarely, as visible conglomerations of fats or fatty acids. The presence of certain undigested vegetable particles is not pathological.

Elements derived from the body itself are pus, blood and mucus. The presence of mucus, and its character, afford very valuable evidence of intestinal conditions. The mucus of the feces is derived partly from the goblet cells of the intestine, the large intestine being incomparably more active in its production than the small, and is partly contained in the bile. It is chemically pure mucin. In its passage through the small intestine it becomes digested and the chyle passes into the colon practically free from it. Under ordinary conditions the feces macroscopically contain no mucus. Hard fecal masses, however, may, during their sojourn in the lower colon, obtain a more or less complete coating of mucus from this portion of the gut, and this offers the only exception to the assertion of Nothnagel that mucus in the feces is invariably an evidence of intestinal "catarrh." According to its form and distribution in the feces very valuable inferences may be drawn as to the seat and nature of the pathological process. Mucus may appear as small, more or less transparent blobs or shreds, or as minute sago-like bodies, or as large semi-translucent jelly-like masses; or under certain well-defined conditions as dense, leathery, tape-like masses. If pure, it is clear, translucent and colorless. Frequently it becomes stained brown by imbibition of feces, or reddish yellow by bilirubin. If admixed with pus or epithelia, it becomes whitish

and opaque. If the feces are solid it never occurs in the interior of the mass, but always as an external coating, in which case it is undoubtedly derived from the large intestine.

Mucus derived from a catarrh of the small gut is ordinarily completely digested and leaves no remnant in the feces, but, under certain conditions, it may be identified, and its origin determined. Thus, if the chyle be driven through with increased rapidity, it often escapes digestion. The feces are then semi-fluid from failure of absorption of its water, and intimately mingled with it are small particles of the mucus. These small particles are apt to be confused with remnants of food, especially of fruits. They are most easily recognized by allowing the stool to flow slowly down the surface of a blackened glass plate. Chemically, they are then easily identified either under the microscope or by the aid of the triacid reaction, with which they stain blue, while proteid constituents stain red. This triacid reaction, which is best applied after rapid fixation of the material in 2.5 per cent. sublimate, fails, unfortunately, to differentiate vegetable material from mucus. The test is very simply applied. A small mass of the suspected material is allowed to dry in the slide, passed through the sublimate, and retained in Ehrlich's triacid until distinctly colored (1-5 minutes), and then washed off.

Certain other characters indicate the origin of this mucus from the higher portions of the intestine; namely, its discoloration by bilirubin and the admixture with semi-digested epithelia or leucocytes. The diagnosis of duodenal or jejunal catarrh from the character of the mucus in the stool is, nevertheless, almost foolhardy; at most, one may say that the finer the subdivision of the mucus and the more intense the bilirubin discoloration, the higher is the seat of the process. The absence of mucus does not, of course, exclude the existence of a catarrh. Very characteristic are the almost leathery, tape-like masses of mucus expelled in muco-membranous colitis. They originate invariably in the large intestine.

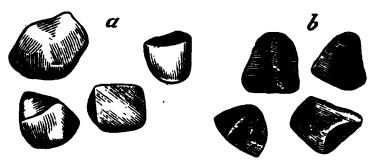
Not only the site, but the character of the process is, to a certain extent, revealed by the mucus. Pure mucus indicates a simple "catarrh;" admixture of pus or epithelia indicates an inflammation; large coherent masses are generally due to a secretory neurosis.

Pus does not appear as a macroscopic constituent of the feces, except in cases of perforation of an abscess into the gut. The pus cells, which occur in the various ulcerative processes, are, with difficulty, recognizable, even microscopically, owing to their digestion

and fragmentation. Blood in the stool is ordinarily recognizable by its color. If it originates high up, it is apt to become much darker through reduction processes during its progress downward. The blood from gastric hemorrhage is usually black and tarry. Hemorrhages from the colon, or even from the lower end of the ileum, as in typhoid, usually stain the stools a far more intense red. Blood derived from the small intestine is usually intimately mixed with the stool, while that from the lower colon or rectum forms an external layer. The miçroscopical examination is generally of little assistance, inasmuch as the corpuscles become greatly altered. If fairly well preserved, their origin from the lower part of the gut may be inferred. The spectroscopic and chemical identifications of blood are treated of in a later section.

Other macroscopic elements are tumor masses, stones, parasites and foreign bodies. Tumor masses rarely appear in the feces; they are derived either from carcinomata or are pedunculated fibro-

FIG. 67.



Gall-stones. (Simon.)
a, cholesterin; *b*, pigment-stones.

adenomata which have broken loose. The former are irregular, crumbly, blood-stained; the latter are firmer and generally rounded. The microscopical examination of frozen sections is often of great assistance in differentiating them from food remnants. Stones are either biliary, pancreatic or fecal concrements. Biliary concrements vary in size from a pea to a pigeon's egg. Smaller stones are, as a rule, dissolved in the intestine. They are generally easily fragmented, and are either reddish brown bilirubin calcium, or whitish and shining (cholesterin). The chemical determination of these constituents is quite simple, and will be subsequently described.

If the stones are larger than a pea, their cystic origin is almost certain; if they are facetted, the existence of numbers of them may be inferred, and if they are only large, there is a cholecystenteric fistula. Frequent sources of error are the so-called "pseudo-gallstones" and inspissated masses of olive oil. Pseudo-gallstones

are similar masses derived from the core of fruits, especially pears. They are much harder than gallstones, differ chemically, and present characteristic "stone cells" under the microscope. Pancreatic stones are rare. They are no larger than a pea, contain no bile pigment, and consist chiefly of calcium carbonate. Coproliths, or fecal concretions, are also rare, and are composed of undigested masses mixed with calcium and magnesium phosphate. The chemical examination of these stones is simple, and proceeds exactly as in case of bladder stones.

Parasites will be described under a special section.

Foreign bodies are not infrequent and are easy of recognition. Notable are the hair balls in young women, similar to gastric bezoares.

CHAPTER XV.

MICROSCOPICAL EXAMINATION OF FECES.

Method.—Microscopical examination of the stools demands a more or less homogeneous semi-fluid condition. Solid stools must, therefore, be rubbed up with a certain amount of water for this purpose. The semi-fluid stools may either be allowed to sediment, and the more solid portions withdrawn by a pipette, or they may be centrifuged. Save in very liquid stools, centrifuging is rarely necessary. The sediment usually settles in more or less distinct layers. At the bottom are the larger crystals, or larger masses of muscles, or heavier vegetable tissues, stone cells, bast fibers, etc.; on the surface are fats and fatty acid crystals and lighter cellulose structures. The process of separation may be perfected by centrifuging first with water acidulated with HCl, then with absolute alcohol, and finally with ether. This removes the alkaline salts, the ethereal oils and chlorophyll, and the fats successively, leaving only the undigested residue, and the acid salts. The microscopical examination is greatly assisted by certain well-known microchemical reactions, which demand the use of the following reagents. These are not essential, but are of much assistance in determining minute detailed structures: Acetic acid, 30 per cent.; potassa, 10-15 per cent. solution, Lugol's solution, Lysol solution, 5 per cent., osmic acid, watery solutions of eosin and methylene blue. Any one of the proteid test reagents, *e. g.*, Millon's.

Meat Residue.—Muscle remnants, recognizable as such, are normally present in all stools after a mixed diet. Their amount depends on the amount of meat in the diet, the kind of meat, and its method of preparation. Tough meats, meats containing much connective tissue, and imperfectly cooked meats are apt to leave a proportionally greater residue. Muscle fragments appear in the feces in size varying from microscopic detritus to macroscopic pieces. When seen under the microscope, they appear either as irregular, polygonal fragments, or more or less rounded. They may be distinctly striated, or entirely homogeneous, in which case their nature must be ascertained by the microchemical reactions. The smaller, the more perfectly rounded, and the more homogeneous they are, the more advanced is their digestion. The frag-

ments are discolored either by urobilin or bilirubin. Even if morphologically unrecognizable, they answer to the various proteid tests, *e. g.*, the biuret, Millon's or the xanthoproteic. Acetic acid causes them to swell up, and brings out the striation; caustic potash dissolves them.

The diagnostic evaluation of the presence of muscle remnants demands much experience. The only accurate tests are those offered by a quantitative estimate after the use of a test meal as suggested by Schmidt, and this is too complicated for routine purposes. The same author states that 100 grammes of browned scraped beef should normally leave no macroscopic residue. If, however, one is convinced that the

FIG. 68. Collective view of the feces. (v. Jaksch.) (Eye-piece, III; objective, 8 A, Reichert.) *a*, muscle-fibers; *b*, connective tissue; *c*, epithelium; *d*, white blood-corpuscles; *e*, spiral cells; *f*, pitted ducts; *g*, cork cells; *h*, parenchyma with starch; *i*, plant hair; *k*, triple phosphate crystals in a mass of various micro-organisms; *l*, stone cell.

muscle remnants are present in excessive amount, the conclusion is inevitable that there is digestive disturbance in the small intestine. The nature of this disturbance, whether secretory, motor, or absorptive, cannot be determined, and it is highly probable that all three factors are in most cases simultaneously concerned. Diarrheas, fevers, amyloidosis, tabes mesaraica, and pancreatic disease are possible causes.

The presence of nuclei in microscopic remnants argues, theoretically, for pancreatic disease. In this connection may be mentioned the use of Sahli's glutoid capsules to diagnose pancreatic disease. This test will be found described in Sahli's text-book of clinical laboratory methods. Capsules are prepared of gelatine hardened in formalin, which are indigestible except in pancreatic

juice. These are filled with iodoform glycerine. The discovery of iodine in the urine or saliva after the administration of one of these capsules is taken to indicate the functional activity of the pancreas.

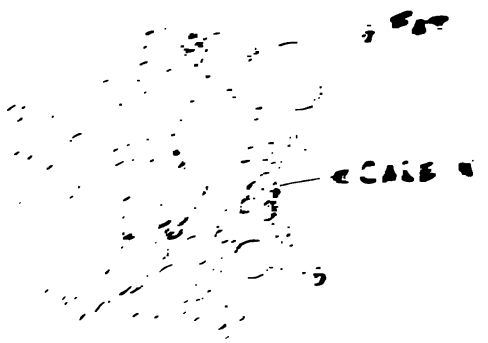
Connective Tissue.—Filaments of connective tissue occur in all feces after a mixed diet. They may either be microscopic, or form considerable masses, which, to the unaided eye, are indistinguishable from conglomerates of fibrin, of vegetable fiber, or of elastic tissue. Microchemically, they swell up and become homogeneous on the addition of acetic acid, whereas the same reagent brings out elastic tissue more sharply, and produces precipitates in mucus. Vegetable fibers may usually be distinguished by their structure, and with certainty, by their not reacting to the usual proteid reactions (xanthoproteic, etc.). There is no diagnostic significance to be attached to the occurrence of connective tissue fibers, unless they are present in large masses; even in this event it is well to be sure that the meat of the food has not been of the "smoked" variety, and has been fairly well cooked, since even normal digestions reject the unaltered connective tissue. Schmidt has asserted, as a quantitative test, that 100 grammes of cooked scraped beef should normally leave no connective tissue residue in the feces. If the tissue be found after such a meal, or be present in large amounts in case of an ordinary mixed diet, it is pathognomonic of disturbance in the gastric functions, since only the stomach possesses the property of digesting this constituent.

Elastic tissue regularly reappears in the feces, being extremely indigestible. It is easily recognized, but has no diagnostic significance.

The presence of a bilirubin stain of connective tissue, and of undigested nuclei, has the same significance as noted in the case of muscle.

Casein.—Of the other constituents of an animal diet, the vast majority leave no recognizable residue in the feces. Those tissues, which were noted in the section on the macroscopic residue as indigestible, reappear, of course, under more or less altered form in the microscopical examination. Fish scales, epidermis, feathers, etc., belong in this category, but most important are the epidermal remains. These latter appear generally as stratified, irregular, more or less refractile elements, and ordinarily possess no nuclei. In the stools of infants, epidermis cells derived either from the mother's breast or from the child's fingers, might cause some confusion.

[illegible]



[illegible] Strasburger.

[illegible] of fat and fat crystals. Microchemically [illegible] react to Millon's reagent, and are dissolved by solution of 5 per cent. hydrochloric acid. They are hardly to be confused with anything except certain minute masses of fatty acid crystals, the nature of which at once becomes clear on microscopical examination.

The diagnostic value of casein stools is made much of by pediatrists. It must be taken, however, only as a symptom of functional disability to cope with the ingested casein, and not necessarily as a sign of organic disorder. Nevertheless,, it offers a valuable dietary indication to alter either the quality or the quantity of the milk.

The same indication holds true in case of adults who, for any reason, are on a milk diet, [illegible] typhoid patients; here the exam-

normal Coloring.

PLATE VIII.

MUSCLE

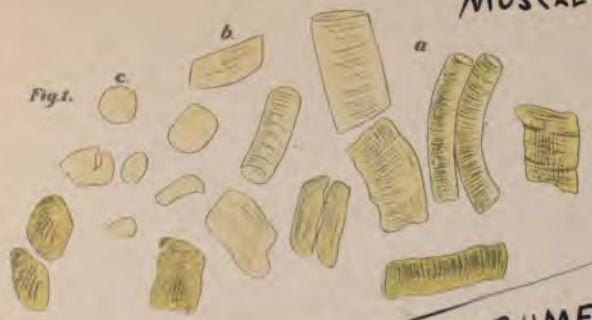


Fig. 1.

Fig. 2

ALBUMEN

CONIUM

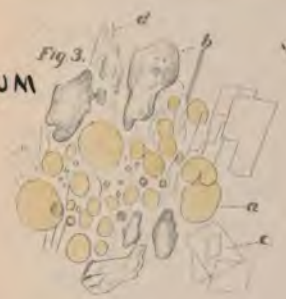
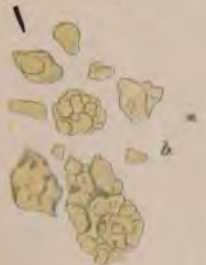


Fig. 3.

SOAP

Fig. 5.



Fat.

Fig. 4

Fig. 1.—Muscle remnants in feces: *a*, large; *b*, medium; *c*, small fragments. (Leitz, obj. 7.)

Fig. 2.—Bile-stained albumin embedded in fecal mucus. (Leitz, 1/12.)

Fig. 3.—Meconium: *a*, meconium corpuscles; *b*, fat; *c*, cholesterin crystals; *d*, epidermis. (Leitz, 7.)

Fig. 4.—Neutral fat: *a*, from the stool of an adult, bilirubin-stained; *b*, from an infant; *c*, stained with osmic acid. (Leitz, 7.)

Fig. 5.—Soap, in crystals and masses: *a*, circle-shaped forms from typhoid stools; *b*, yellow calcium salts. (Leitz, obj. 7.) From Schmidt and Strasburger.

ination of the feces for casein is necessary to determine whether the diet is accepted as food or not.

Vegetable Proteids.—Vegetable proteids, such as occur in certain vegetables, fruits and particularly in nuts, are a highly digestible and nutritious element of the diet in themselves. Being inclosed within a cellulose envelope, however, they often pass through the intestinal canal unaltered, and are then discovered microscopically or microchemically.

In most seeds, pea, bean, nuts of all kinds, the vegetable proteins are largely massed into crystalline form, making up the aleurone grains. These are very prominent in many seeds, and are even sufficiently characteristic to offer considerable aid in the diagnosis of the particular class of food ingested or undigested. As a rule, however, the aleurone grains are soluble in water, and are very readily dissolved out of the cell membranes, even though these latter are unbroken. In acute diarrheal conditions, particularly of the motor variety, unaltered aleurone grains may be found in foods of the type mentioned.

Observations regarding the solubility of these grains in pathological fluids, such as the serous discharges of fermentative diarrheas, are wanting. Such might offer an attractive field for research.

Fats.—Necessary to an appreciation of the fats and their derivatives, and of their diagnostic significance in the feces, is an understanding of the chemistry of these compounds. The fatty components of the food are almost entirely in the form of neutral fats. These are technically triglycerides of the fatty acids. Glycerine is an alcohol containing three hydroxyl groups, having the formula $C_3H_5(OH)_3$. When the fatty acids unite with the alcohol radical, they displace the hydroxyl groups, and a neutral fat is formed. The chief of these, as found in the food, are olein, palmitin and stearin, which occur as the chief fats of the animal body. Other fatty acids which combine to form fats are caproic, butyric, and others. The vegetable oils contain a far greater proportion of uncombined fatty acids than do the animal fats.

The digestion of fats consists of a series of operations in which different parts of the alimentary tract severally take an important share. In the stomach the splitting of fats is begun through the agency both of micro-organisms and of a recently-discovered ferment. In the duodenum the fats are finely emulsified by the bile, and then split up by the steapsin of the pancreatic secretion into glycerine and fatty acids. The acids remain in part as such, in part unite with the salts of the alkalies present, sodium, potas-

sium and calcium chiefly, to form soaps. These soaps and salts then pass into solution in the bile, and are so absorbed. Neutral fats cannot be absorbed, nor can soaps or fatty acids in the absence of bile. It will thus be seen that an analysis of the stools with reference to the diagnostic significance of their fat contents is no simple matter.

Fat occurs in all feces, normal and pathological, and may be recognized in the form either of neutral fats, soaps, or fatty acids. Fatty stools, *e. g.*, the "fat diarrheas" of infants, are recognizable as such macroscopically, by their whitish color, often a peculiar sheen, and in liquid stools by the presence of a thin floating layer of fatty acid crystals.

Neutral fats appear either as droplets or as masses with irregularly-rounded contours. This difference depends in a difference in

FIG. 70.

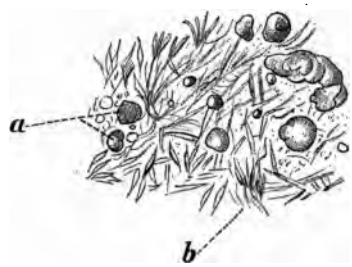
Crystals of the fatty acids. *a*, mingled with mucus; *b*, around fat droplets in an infant's stool to which glycerin has been added. (From Schmidt and Strasburger.)

melting points, the former having the lower point. The droplets are colorless, the irregular masses more or less deeply bile-stained. Microchemically, the neutral fats are insoluble in water, barely so in cold alcohol, soluble in ether, chloroform and hot alcohol. Osmic acid stains them a dense black; this, however, is strictly true only of the olein fats, the other forms must first be treated with alcohol, and then stain a rusty red to black.

The fatty acids, such as butyric acid, are in part volatile, and rapidly evaporate from the feces. The lower forms occur both as amorphous masses, similar to those composed of neutral fats, and as crystals. The crystals are generally sheaves of very delicate, point-tipped, needles. Microchemically, they may be identified by their solubility in cold alcohol. The crystals are always free from biliary coloring matter. With osmic acid they stain coarsely and irregularly black.

The soaps occur microscopically either as amorphous masses, or crystals. The amorphous masses may be colorless, or stained by biliary pigments. Their contour is said to present more angularities than do those of fats or fatty acids. The crystals are generally in the form of colorless needles, often arranged in sheaves,

FIG. 71.

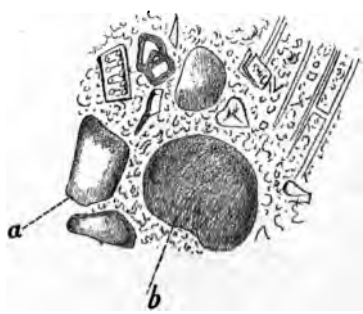


a, fatty acid amorphous masses; *b*, soap crystals. (From Schmidt and Strasburger.)

and are shorter, broader and blunter than those of the fatty acids. Another form described resembles the egg of *Tænia*.

Microchemically, one must distinguish between the calcium salts which constitute the greatest portion of the soaps, and the salts of the alkaline metals. The former are insoluble in hot water, alcohol or ether, and do not stain with osmic acid or Sudan red.

FIG. 72.

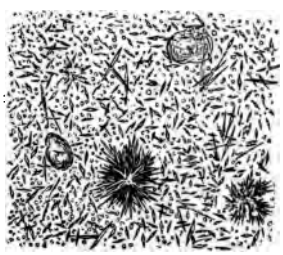


a, masses of soap; *b*, Nothnagel's "islands of hyaline mucus."
(From Schmidt and Strasburger.)

On heating they do not change to droplets, as do the crystals of fatty acids and the neutral fats. If they are warmed in the presence of acids, fat droplets are formed, simultaneously with the corresponding salt of the acid introduced. The latter differ in that they are soluble in hot water and alcohol.

The pathological significance of fats in the feces can be understood only with reference to normal conditions. Thus in infants, owing to an incomplete development of the fat-splitting function, there is always a considerable amount of fat in the stools, which decreases as the child grows older; fat droplets, crystals and amorphous masses are all present. Biedert has described a "fatty diarrhea," in which the fats are a preponderant element in the stools, and this is certainly pathological even in infants. In adults, it is rare to find neutral fat droplets, except after the ingestion of large amounts of oils of low melting point, as olive oil or castor oil. Normally, fats occur in small amounts as amorphous masses of soaps, more rarely as crystals. The presence of large amounts of neutral fats is always pathological, and is betrayed even macroscopically by the glistening, soft character of the stool, with a whitish tinge.

FIG. 73.



Feces of jaundice. (v. Jaksch.)

Fatty acids have been found by Herter in large amounts in the feces, as the splitting of fats into glycerine and the fatty acids may take place energetically in the lower part of the small intestine under the influence of organisms of the colon bacillus group.

The exact nature of the disturbance must be gathered from other signs, inasmuch as increased peristalsis, amyloidosis, biliary obstruction and pancreatic disease all interfere with the absorption of fats. The distinction, however, is generally easy to make between these conditions.

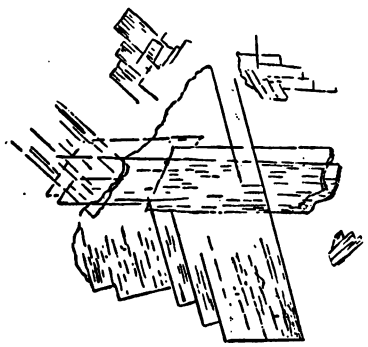
In pancreatic disease there is not necessarily so much a quantitative increase in fats as a qualitative change, inasmuch as the exclusion of the pancreatic fat-splitting enzyme (steapsin) from the gut leads to the presence of a far larger proportion of neutral fat. In biliary obstruction, on the other hand, although complete splitting takes place, there is a diminution of the absorptive function, inas-

much as the bile acts as the vehicle or solvent of soaps and fatty acids, hence a preponderance of the latter in the stool.

Crystals.—A variety of crystalline salts occur in the feces, especially the phosphates, and magnesium and calcium salts. They have no diagnostic significance, and present the same morphological and microchemical reactions as already described for the urine.

Cholesterin occurs in characteristic form, and is frequently found in the stools of infants. Charcot-Leyden crystals seem to occur with especial frequence in cases of helminthiasis and of mucus colitis, although occasionally in other conditions also. They are found in greatest number in the mucus itself. The crystals are apparently identical with those found in the sputum; colorless octahedra, with sharp margins, and generally broken angles. Their

FIG. 74.



Cholesterin crystals. (Simon.)

genetic relationship with the above named pathological conditions is not clear.

Hemin crystals probably are not to be found, but those of hematoidin occur occasionally either as needles, rhombs, or amorphous masses of reddish-brown color. They seem to be especially associated with hemorrhages into the bowel or stomach, either from ulceration or congestive catarrhs.

Similar in appearance, but of a lighter color, are the bilirubin crystals, which occur not infrequently in the diarrheal stools of adults. The latter are easily distinguished by their microchemical reactions, as elsewhere described.

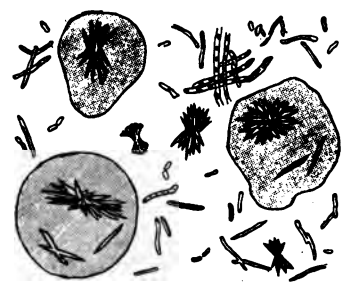
Crystals from vegetable foods are very numerous and characteristic. These are for the most part made up of calcium oxalate. Calcium carbonate crystals are also found in many vegetables.

For microscopical purposes, however, only the calcium oxalate crystals need be considered.

In general three prevailing types of these crystals are found. Needle shaped (raphides), rosette forms, and rhomboids. Frequently these three may be associated in the same plant, but at times only one form may be present; rosettes, for instance, in rhubarb.

In cases of markedly-increased acidity of the gastric juice (HCl), the calcium oxalate crystals may be dissolved, but otherwise they form a constant feature in the stools of a mixed diet, including green vegetables. A certain amount of the calcium oxalate is absorbed under most conditions. Occasionally, as seen in the chapter on urine, oxaluria is present, as a result of either increased ingestion of vegetable food containing large amounts of calcium

FIG. 75.



Hematoidin crystals from the feces. (v. Jaksch.)

oxalate; increased gastric acidity, rendering more soluble that which has been ingested; oxidative metabolic defects, as yet imperfectly understood (see urine oxaluria), by which complete oxidation of the oxalic acid does not take place.

From a medico-legal point of view, a large chapter on plant crystals might be written, as practically all of the narcotic poisons, aconite, belladonna, digitalis, hyoscyamus, etc., when taken in their crude state leave residues either in the gastric contents or feces, which are identifiable largely from the plant crystals.

Mucus.—The characteristics of mucus have been more or less fully described in the macroscopic section. Minute particles of mucus, such as are usually identified with catarrh of the upper bowel, may be most easily detected if the stools be mixed with water and allowed to trickle down the surface of a blackened plate of glass. Microscopically, it appears as more or less homogeneous,

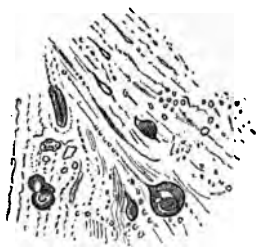
transparent masses, with faintly marked contours. It may occur as pure mucus, or mingled with leucocytes, epithelia, blood or food detritus. There may be slight discoloration by biliary pigments.

The most characteristic microchemical reaction is that with acetic acid, which precipitates the mucus, producing at the same time irregular linear markings; the same reagent "clears" the cells, and brings out their nuclei sharply.

The diagnostic features of mucus are thus summarized by Schmidt and Strasburger:

1. If the mucus be densely impregnated with bacteria, detritus and food remnants, this speaks for its origin high up in the intestine.

FIG. 76.



Mucus shreds.
(From Schmidt and Strasburger.)

FIG. 77.

Mucus shreds after the addition of acetic acid.

2. Bilirubin discoloration affords no certain evidence of catarrh of the small intestine, but the presence of bilirubin granules and crystals in a cellular arrangement may be interpreted in this sense.

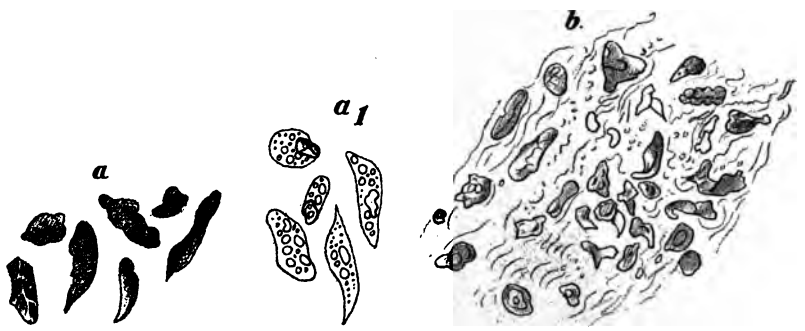
3. The presence of semi-digested cells, or of their nuclei, indicates a high origin.

4. The presence of hyaline cells argues strongly for colon catarrh. Mucus unmingled with epithelia or pus cells indicates a far lower degree of inflammation than the opposite condition.

Epithelium.—Epithelia form a constant constituent of all feces, owing to the continual attrition of the intestinal contents, and

perhaps to a spontaneous process of desquamation. Normally, however, they are so mingled with the feces, and generally so altered by digestion, that special attention must be directed to them in order to identify them. In catarrhal or dysenteric processes, however, they constitute a very prominent and important element. This is in striking contrast with the leucocytes which play but a small part in coprologic diagnosis. The conditions are thus the reverse of those which maintain in the sputum. Epithelia are of various types, according to the area of the tract from which they originate; those from the anus belong to the stratified squamous type, while those from the intestine are cylindrical. It is only rarely, however, that epithelium is passed out in a condition resembling at all closely that which it normally shows. Not only is

FIG. 78.



The so-called "Verschollte Zellen." *a*, unaltered; *a1*, after the addition of acetic acid and heat; *b*, in the mucus from the colon. (From Schmidt and Strasburger.)

it subject to the action of the various digestive juices in its passage through the gut, but the original intestinal epithelium may be in a degenerative condition. Thus it is important to recognize fully degenerated cells, which are often swollen to three or four times their ordinary size; semi-digested cells, with ragged contours, clouded protoplasm, and, at times, only the remains of a nucleus, and a peculiar type known to the German describers as "Verschollte Zellen," with an amyloid or starchy appearance. The last named form is very frequently seen, especially in connection with mucus. The cells are small, homogeneous, possess no nucleus, and show increased refractile power as seen through the microscope, like amyloid. They were long considered to represent this type of degeneration, until it was shown that the appearance is due to an imbibition with soaps. This imbibition in all probability repre-

sents not a vital cellular process, but a postmortem change of the cell, and is seen also in leucocytes. This form of cell is considered to indicate its origin from the large intestine.

Epithelial cells occur in all inflammatory conditions of the intestine, and are generally imbedded in the mucus. If large masses of mucus are passed without a corresponding dejection of epithelia, the condition is almost certainly neurotic, "enteritis membranacea," and not inflammatory.

Large masses of coherent cells, fairly well preserved, occur in toxic enteritides, with rapid passage of the intestinal contents, and in cases of strangulated intussusceptions. In general, the further digested the epithelia, the more probable is their origin from the small intestine. This probability becomes almost a certainty when these cells are imbedded in small clumps of mucus.

Leucocytes.—The same alterations which disguise the epithelial cells are found in the leucocytes in the feces. Normally,

FIG. 79.

Degenerated intestinal epithelium. (v. Jaksch.)

they may be found in small numbers in every stool. In catarrhal processes, whether acute or chronic, they are but slightly increased, and do not constitute nearly as prominent a feature of these conditions as do the epithelial cells. Their presence in greater numbers indicates an ulcerative affection.

Pus in very considerable amount in the stool points to the rupture of an extra-intestinal abscess into the gut, and the better preserved the leucocytes, the lower down may this be located.

Eosinophiles occur in the feces in a few conditions, notably helminthiasis and muco-membranous colitis. They are recognized by their affinity for eosin, any one of the ordinary blood stains being available for the test. The rationale of their presence is not understood. Possibly the eosinophilia is related to that which occurs in

the blood in many cases of helminthiasis, while the eosinophiles in the stools of colitis membranacea may be compared to those found in the sputum in asthma.

Erythrocytes.—Red blood cells, unless derived from the lower colon, are generally distorted beyond recognition in the feces; occasionally, "shadow corpuscles," which preserve the form, but not the color, may be found. If there is, however, a simultaneous diarrhea, the cells may be fairly well preserved.

The detection of blood traces forms a very important chapter of the chemical examination of the feces, and will be there described.

Diagnostically, fecal masses presenting external streaks of blood point towards bleeding hemorrhoids. Microscopic traces of blood in typhoid often precede larger hemorrhages.

FIG. 80.

Fibrin coagula. (From Schmidt and Strasburger.)

Tumors.—Masses of intestinal tissue but rarely slough off, as in cases of intussusception. Occasionally particles of hemorrhoids come away. Carcinoma and adenoma occasionally part with sloughs, which may be examined either by means of scrapings or by microscopic sections. Polypi are sometimes passed complete.

Nothnagel's Bodies.—Nothnagel, in 1884, described a form of mucus in the stool, which he considered characteristic of ileitis. It occurs in minute granules, bordering on the limits of the macroscopic in size, the largest being of the size of the head of a pin. They vary in number, and in some cases are so numerous that the entire fecal mass, which then becomes almost fluid, simply swarms with them. They are yellow to brown in color. Their consistency is soft, and when crushed under a cover-glass they spread out in a homogeneous mass. They never contain epithelia or round cells.

Through work of Schorlemmer and of Schmidt, it is now quite clear that these bodies are not composed of mucus, but of albumin. The fact, however, that the bodies are generally imbedded in small shreds of mucus, and that they are colored with bilirubin, lends them the same diagnostic significance as was originally attributed to them by Nothnagel, namely of an ileitis. Bilirubin, as has been said, occurs normally only in the ileum and never in the colon, and can only be found in the feces in case the peristalsis of ileum and colon is abnormally active.

Meconium.—During the first two days of infant life a material is passed out of the rectum which differs both in origin, composition and physical characteristics from the ordinary stool of the infant. This so-called meconium is of an olive color, soft, and is passed four to six times daily. It is composed of intestinal secretions and epithelial cells, of mucus, of bile, of hairs, and of fat globules. Microscopically, there are epithelia in various stages of degeneration, cholesterin crystals, fats and the so-called meconium corpuscles. The latter are homogeneous, rounded globules, of a yellowish color. Their origin is uncertain, but they are in all probability albuminous in nature.

VEGETABLE DETRITUS.

The microscopical examination of the vegetable detritus in the feces is beset with many difficulties. This is not due so much to the changes induced by the various digestive processes, but more particularly to the great similarity that exists in the various plant cells that are so constantly used as food.

In the present stage of its development, it is unquestionably true that very little information of a directly applicable character has been gained from the study of the vegetable remains in the feces. This has been due very largely to the fact that when compared with the wealth of detail obtained by other methods, the feces have very rarely been examined by the student of plant histology, and when so studied the rarer combination of gastro-enterologist and histologist has been lacking.

The microscopical investigation of many of the common food products has been carried on by experts for years, but the point of view has almost always been that of the hygienist, who in his studies has been keenly alert to detect adulterations in foods. From this standpoint the study has been pursued with infinite

detail. Such works as Vogl,[1] Wiesner,[2] Meyer,[3] Hanausek[4] and Greenish,[5] represent the best of the kind in any literature, and all testify to the intrinsic interest that studies of this kind possess, particularly from the standpoint of the sanitary expert on foods. Such works represent even a wider field, for their pages are filled with information directly applicable to the needs of the microscopist who would study the feces. It would seem that van Ledden Hulsebosch (1899) had been almost the only investigator to fully follow out these methods.

These authorities have been here quoted in this manner, since the methods pursued in these volumes are the methods which must be followed by the student of the feces if definite conceptions regarding the action of the gastro-enteric tract upon the food are to be gained. It will not take many years before a mass of practical data can be accumulated if studies of this type are prosecuted.

It is well known that the cells of plants differ very widely from those of animals in the possession of a distinct cell wall. This cell wall is composed largely of cellulose, or a modification of the same, or of a mixture of cellulose and modifications, variously termed cutin, suberin, lignin, etc. Cutinized cell walls are characteristic of the peripheral walls of plant organs of all kinds, leaves, stems, etc. Suberized cell walls are present in corky tissues; whereas lignified cell walls are present in stone cells, in various ducts and tracheids, and in wood fibers and in bast fibers.

The substances causing these modifications are very imperfectly understood at the present time, and, while their microchemical characters in an unaltered condition are well known, very little is understood concerning these same microchemical characters after digestion.

All of these modifications render cellulose much more unalterable than when in its original condition, and in certain vegetables and fruits many cells with walls of these characters are encountered.

Ordinary cellulose is not as indigestible as has been taught, and it is by no means the exception to find the cellulose walls in many

[1] A. E. Vogl, Die wichtigsten vegetabilischen Nahrungs und Genussmittel mit besonderer Berücksichtigung der mikroskopischen Untersuchung auf ihre Echtheit, ihre Verunreinigungen und Verfälschungen. Vienna, 1889.

[2] J. Wiesner, Die Rohstoffe des Pflanzenreiches, 2d edition, 1900.

[3] A. Meyer, Die Grundlagen und die Methoden für die mikroskopische Untersuchung von Pflanzenpulvern, 1901.

[4] Lehrbuch der technischen Mikroskopie 1901

[5] Greenish, Foods and Drugs 1903.

vegetables broken down by the digestive processes, especially when the masses of cellulose are not too bulky. This fact was maintained as early as 1870 by Weiske (Ztsch. f. Biologie), but has frequently been overlooked. The microchemical tests are also somewhat altered in many instances; instead of the pure light blue caused by the addition of iodine and sulphuric acid to cellulose, an aborted reaction takes place. Often the cellulose residue is much more soluble in copper oxyammonia solution than when acted on before the digestive processes have been active. Quantitative tests have not yet been found reliable to indicate any particular grade of digestive function.

The action of weak alkalies (NaOH) on cellulose is to convert it partly into meta-arabic acid. This is partly soluble in water, and is possibly a part of the reaction that occurs in cellulose digestion microchemically.

Just what processes take place in the intestines whereby simple cellulose is digested are not as yet thoroughly understood. Tappeiner, Prausnitz and a score of others have endeavored to determine the causes. It has been known for years that under the actuation of certain enzymes in germinating seeds the cellulose membranes swell, become converted into a soluble carbohydrate, and as such contribute to the nutrition of the young plant. The breaking down of cellulose, and even lignified cellulose, as found in wood (railroad ties, etc.), by moulds from the activities of cytases is a common every-day phenomenon, and it is further observed that certain lower organisms, yeasts and bacteria are capable of reducing cellulose to a soluble modification.

The production of cytases in the intestinal canal has not been observed, but some degree of hydrolysis of the cellulose does occur. Whether this is due to the enzymes of normal intestinal bacteria, to alkalies, or to other vital ferment action is not yet certain.

In normal digestion, however, it is found that the parenchymatic cells of those tissues which are young, and whose cell walls are very delicate, are found in the feces either to have been completely broken down, or sufficiently digested to permit ready breaking down of the cellular masses and the digestion of the cell contents.

In mild, constipated states it has been observed that the cellulose walls have shown a greater degree of splitting, and it has been inferred that the prolonged stay in the large intestine has permitted more extended hydrolysis, presumably from bacterial action, and hence more cellulose modification. On the other hand, in diarrheal conditions, notably in irritative conditions of the small

intestine in contradistinction to colitis, the grade of cellulose disintegration is distinctly less advanced, and the food plant cells, as found in the feces, show little alteration on comparison with the source in their fresh condition.

Moeller[1] first pointed out that, whereas only thin cellulose walls were broken down in the digestive process, the pectin-like substances which constitute the middle lamellæ of plant cells was almost invariably attacked, much as if they had been acted on by the well-known histological maceration agents, such as Schultze's. This permits the falling apart of the cells in any mass of tissue, and thereby aids the further digestion of the individual cells.

This characteristic reaction offers another slight help in the interpretation of digestion. Thus the masses of cells are greater in those passages that have been hurried through the intestinal canal—a fact already known macroscopically.

The microchemistry of cellulose offers little. In diarrheal states, the iodine (Iodine (1), K. I. (2) Aq. 200) sulphuric acid test (Conc. H_2SO_4) may show little alteration of the cellulose. This test may not reveal any cellulose in the constipated stool. Chloriodide of zinc imparts a distinct violet tone to simple cellulose walls, and reveals similar facts. Szydlowski[2] thought by microchemical tests to simplify the question markedly, but beyond the few facts already pointed out, it cannot be said that his results have been verified. The test of solubility of the cellulose in the copper oxyammonia reagent is not readily applicable in this line of research.

As for the results obtained from the study of cell contents, only the observations concerning chlorophyll, starch, aleurone grains, and crystals, seem of value.

As to chlorophyll, it is frequently entirely destroyed in the intestine. When such vegetables as spinach, beet tops, etc., are eaten, and in comparatively large quantities, abundant evidences of unaltered chlorophyll grains are found in the feces. Moeller (l. c.) says that he has never demonstrated the presence of assimilation starch in the chlorophyll grains in these cases, although the fresh vegetable contains it in abundance. The significance of this test as an index of digestion has never been worked out. The presence of such grains in the chlorophyll would argue a loss or reduction in the amount of pancreatic diastatic ferment.

Starch is the most characteristic formed element in most food

[1] Ztschft. f. Biologie 17, 1897, p. 306.

[2] Beiträge z. Mikroskopie der Feces. Breslau Dissertation. 1879.

products. It is almost always digested in the normal process, even when it may be taken in comparatively large masses, such as rice grains or sliced potatoes. In normal digestion most cereal starches also show digestion. They are swollen if present at all, and do not show the typical blue reaction to weak iodine-potassium iodide solutions. In mild diarrheal conditions and in conditions associated with diminution of the pancreatic ferments, unchanged or only slightly modified starch is present.

Starch in the well-known form of microscopic granules, with concentric or eccentric markings, is rarely seen in the normal stool, except when large amounts of raw or partially-cooked starch have been included in the food. On the other hand, starch masses enclosed in cellulose membranes are not infrequent. The partially-digested, dextrinized granules of starch, such as occur in normal stools, are, for the most part, no longer recognizable microscopically by their structure, and must be identified by their chemical reactions. The most characteristic of these is the blue coloration with iodine, generally employed in the form of Gram's or Lugol's solution. The semi-digested particles, "erythrodextrins," stain a mahogany brown to reddish, while the final stages do not become discolored by iodine. In performing the test, it is necessary to bring about an intimate admixture of the chemical and the feces.

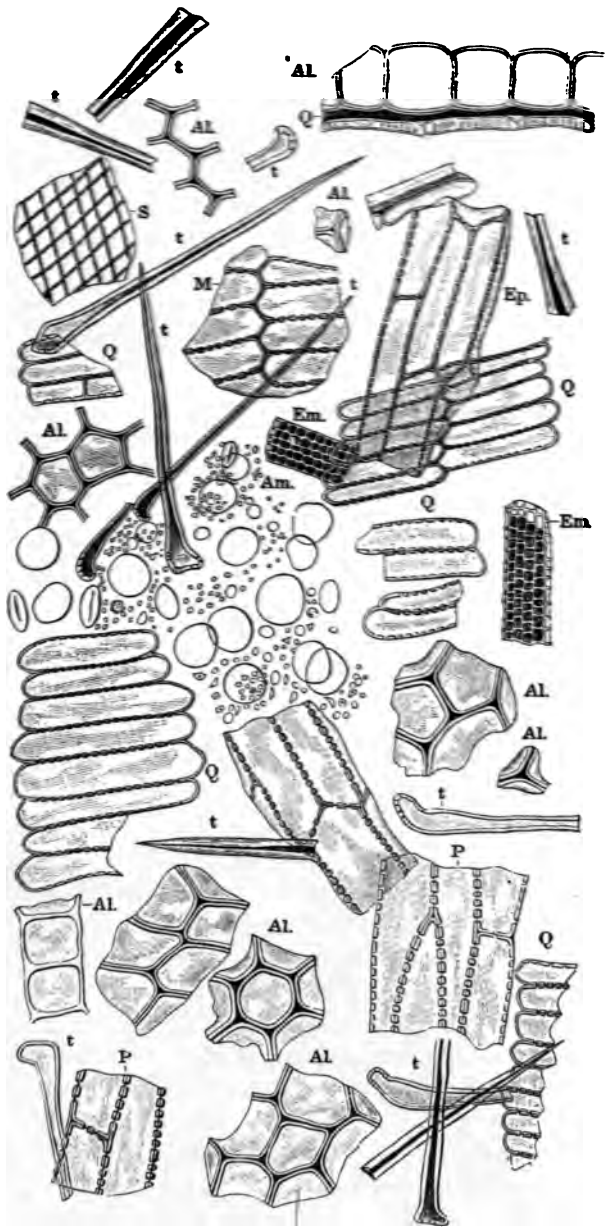
Diagnostically, the presence in the stools of unaltered starch grains, except as enclosed in plant cells (cellulose), is a rarity under normal conditions. If isolated unaltered starch granules occur in any amount, one may argue a disturbance of digestion. The disturbance is localized in the small intestine, and is always severe in character. In searching for starch, care should be taken not to fragment the undigested vegetable particles which occur in most stools, thus, perhaps, setting free starch granules which were originally enclosed in a cellulose membrane.

In the more commonly used cereals and starchy foods, the starch grains are of characteristic shapes, so much so that in the unaltered condition their source may be recognized after the passage of the intestinal canal.

The accompanying table of classification, adapted from Vogl, and from Wiesner[1] may serve to identify some of these more important starches.

[1]Mikroskopische Technologie.

FIG. 81.

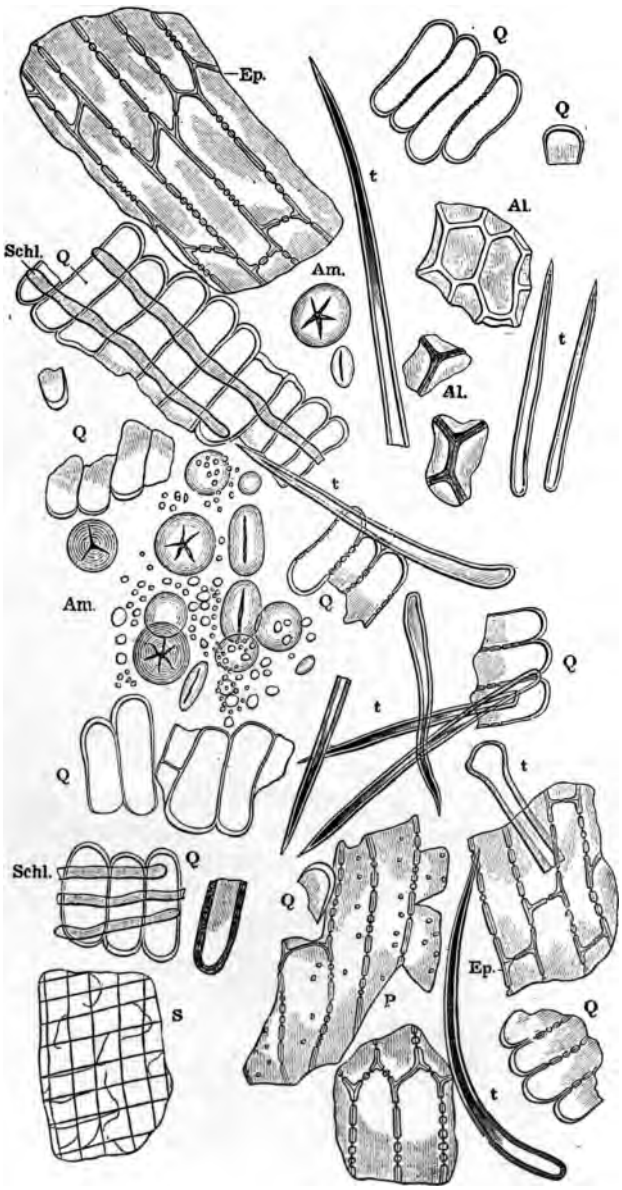


The elements of wheat flour. Ep, epidermis; M and P, middle layer; Q, cells lying outside of hypodermis; S, seed coat; Al, aleurone cells; t, hairs; Em, cotyledon tissue; Am, starch. (Vogl.)

A. Granules simple, bounded by rounded surfaces.
  I. Hilum central, layers concentric.
    a. Mostly rounded or from the side, lens-shaped.
      1. Large granules, 0.0396-0.0528 mm. Rye starch.
      2. Large granules, 0.0352-0.0396 mm. Wheat starch.
      3. Large granules, 0.0264 mm. Barley starch.
    b. Egg-shaped, oval, kidney-shaped. Hilum often long and ragged.
      1. Large granules, 0.032-0.097 mm. Leguminous starches.
  II. Hilum eccentric, layers plainly eccentric or meniscus shaped.
    a. Granules not at all or only slightly flattened.
      1. Hilum mostly at the smaller end, 0.06-0.010 mm. Potato starch.
      2. Hilum mostly at the broader end, or toward the middle in simple granules, 0.022-0.0600 mm. Maranta starch.
    b. Granules more or less strongly flattened.
      1. Many drawn out to a short point at one end.
        a. At the most 0.060 mm. long. Curcuma starch.
        b. As much as 0.132 mm. long. Canna starch.
      2. Many lengthened to bean-shaped, disk-shaped or flattened; hilum near the broader end, 0.044-0.075 mm. Banana starch.
      3. Many strongly kidney-shaped; hilum near the edge, 0.048-0.056 Sisyrinchium starch.
      4. Egg-shaped; at one end reduced to a wedge, at the other enlarged; hilum at the smaller end, 0.05-0.07 mm. Yam starch.

B. Granules simple or compound, single granules or parts of granules, either bounded entirely by plane surfaces, many angled, or by partly-rounded surfaces.
  I. Granules entirely angular.
    1. With a prominent hilum. At most 0.0066 mm. Rice starch.
    2. Without a hilum. The largest 0.0088 mm. Millet starch.
  II. Among the many angled, also rounded forms.
    a. Few partly-rounded forms present, angular form predominating.

FIG. 82.



Rye flour. Ep, epidermis; P, middle layer; Q, cells outside of hypoderm; S, seed coat; Al, aleurone cells; t, hairs; Am, starch; Schl, fragments of bladder-like cells near Q. (Vogl.)

1. Without hilum or depression, very small 0.0044 mm. Oat starch.
2. With hilum or depression, 0.0132-0.0220 mm.
   a. Hilum or its depression considerably rounded; here and there the granules united into differently-formed groups. Buckwheat starch.
   b. Hilum mostly radiatory or star-shaped; all the granules free. Corn starch.

b. More or less numerous kettledrum and sugarloaf-like forms.

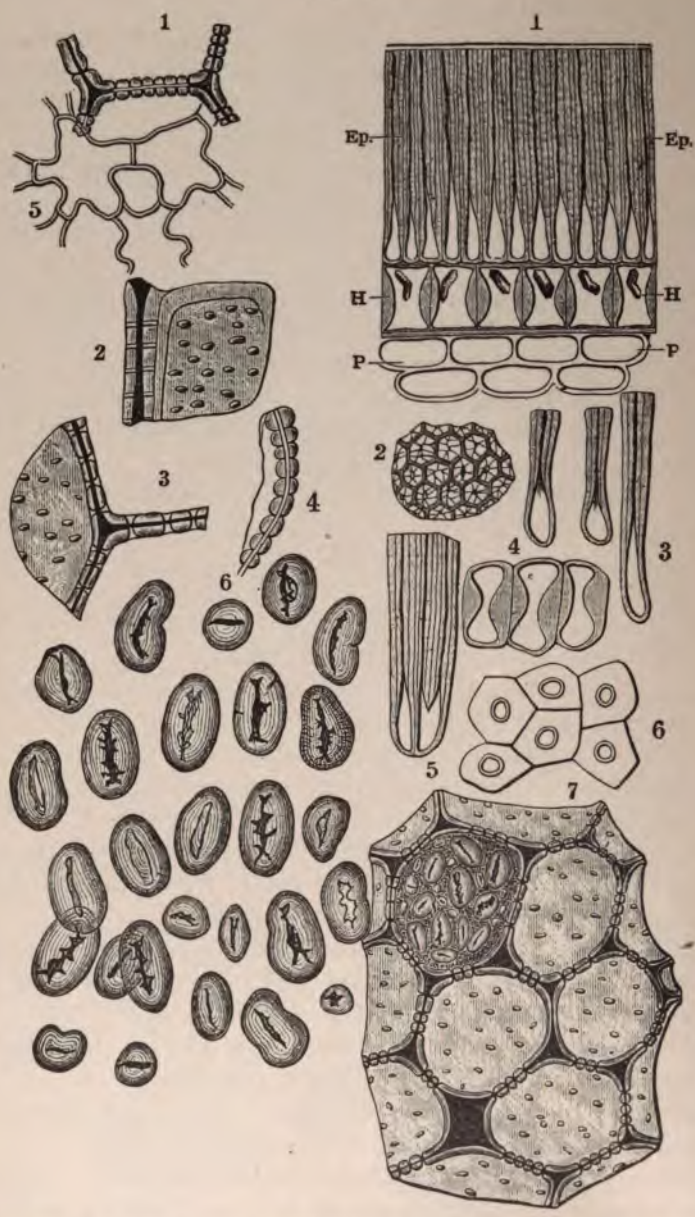
1. Very numerous eccentric layers; the largest granules 0.022-0.0352 mm. Batata starch.
2. Without layers or rings, 0.008-0.032 mm.
   a. In the kettledrum-shaped granules the hylar depression mostly widened on the flattened side, 0.008-0.022 mm. Cassava starch.
   b. Depression wanting or not enlarged.
      aa. Hilum small, eccentric, 0.008-0.016 mm. Pachyrhizus starch.
      bb. Hilum small, central or wanting.
         aaa. Many irregular forms, 0.008-0.0176 mm. Sechium starch.
         bbb. But few angular forms; some with radiatory hilal fissure, 0.008-0.0176 mm. Castanospermum starch.

C. Granules simple and compound, predominant forms egg-shaped and oval, with eccentric hilum and numerous layers, the compound granules made up of a large granule and one or more relatively small kettledrum-shaped ones, 0.025-0.066 mm. Sago starch.

The legumes, peas, beans (lima and white) show unmodified starch even after healthy digestion. In these, especially if not very much broken up, the seed coat prevents the full action of the digestive processes. The unripe seeds show a better digestion than the ripe ones, especially if the latter have been dried. In both pea and bean the epidermis cells and a row of bottle-shaped cells beneath are unaltered. These are strongly cutinized.

From a practical point of view it is apparent that in digestive disturbances it is highly improbable that the green vegetables are of much value. Their food value is relatively low, and, in view of the fact that the microscope shows unaltered cell walls, it is probable that they are only admissible when given in a very

FIG. 83.



Bean flour. 1, to right, cross section of testa; Ep, epidermis palissade cells; H, hypoderm with calcium oxalate crystals; P, parenchyma; 2, epidermis cells in flat; 3, 5, isolated palissade cells; 4, hypoderm cells in profile; 6, same seen flat; 7, tissue of cotyledons. Left, 1-4, cotyledon cells; 5, reticulated parenchyma of seed coat; 6, starch. (Vogl.)

finely-divided condition. The outer coat of the pea, bean and cereals all come within this restriction particularly.

Aleurone grains being very soluble in water are usually taken up readily, from the seeds of which, in many instances, almonds, they make the larger part. In blood serum aleurone grains do not seem to dissolve, and hence they are found in the feces after serous diarrheas and dysenteries in slightly altered form only. Up to the present time research has overlooked the aleurone grain very largely.

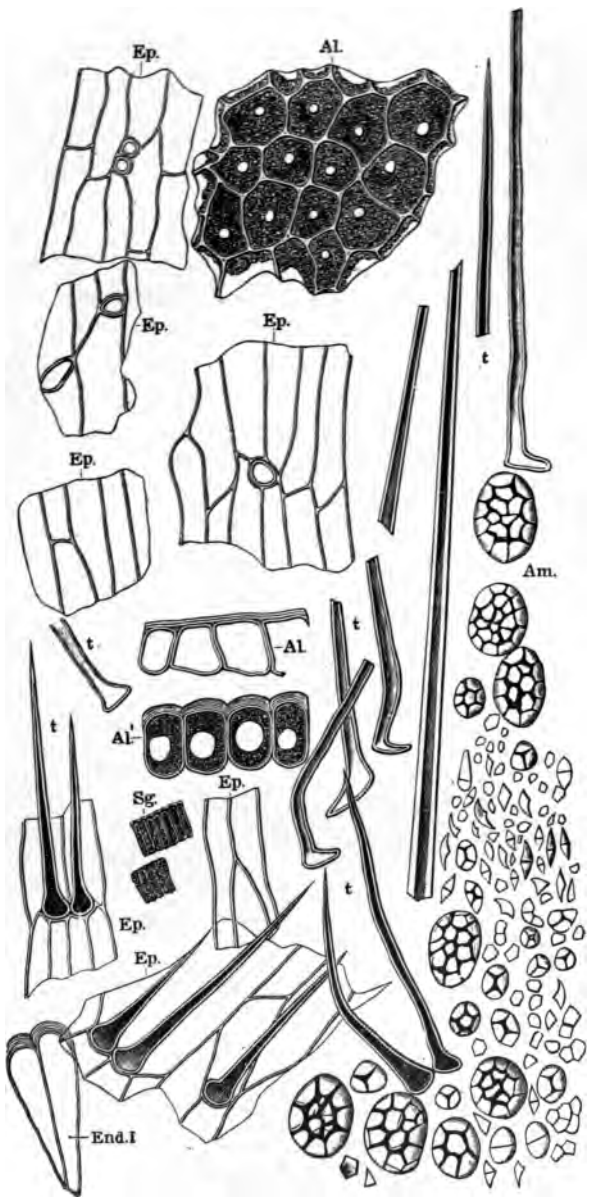
Crystals of calcium oxalate are abundant in most food plants, being particularly rich in rhubarb, beet tops, tomatoes, spinach and many greens. Their fate is not entirely worked out. Many are dissolved in the acid gastric juice, particularly in hyperchlorhydria, and thus are absent in the stools, and appear as oxalates in the urine. They are found abundantly in the feces in those conditions in which cellulose disintegration is retarded, as they cannot escape from the plant cells in which they are imprisoned. Rosette crystals, rhomboids, and acicular varieties are those most commonly met with. Rhubarb crystals are large rosettes.

In normal feces the cutinized elements, notably the epidermis cells, with hairs and stomata, are readily recognized. They are rarely altered, especially if the epidermal walls are thickened. The same is true of the lignified elements in plant tissues. Those found in practically all plants are the ducts—spiral, reticulated and pitted. The presence of pitted and reticulated ducts in the feces invariably means that the vegetables have been over-ripe and old, becoming woody, as is often the case with beets, carrots, turnips, cucumbers, etc. In fresh, green vegetables practically only the more delicate spiral ducts are to be found. With increasing age the pitted and reticulated ducts appear. Celery invariably contains the stronger lignified ducts, and they are abundantly found in the feces after eating celery.

From the diagnostic point of view, it is doubtful if, in our present state of knowledge, much can be learned of the digestive processes from the study of these lignified elements. The slight cellulose wall in the spiral vessels may be completely disintegrated, freeing the more resistant spiral thickening, but this offers little help as an index to digestive function.

Much concerning plant detritus may be gained from systematic microscopical examination of the feces, particularly from the medico-legal standpoint. Diagnosis of poisoning by many mineral and vegetable poisons may be made thereby. This is partic-

FIG. 84.



Oat flour. Ep, epidermis; Al, aleurone cells; Al¹ the same after treatment by NaOH; t, hairs; Am, starch; Sg, epidermis fragments; End, cells from endosperm. (Vogl.)

ularly true in the case of poisoning by the vegetable narcotic poisons, belladonna, aconite, etc., etc., The identification of these poisons rests on a thorough knowledge of the cell elements of the plants themselves. This lies outside of the scope of the present work, but reference may again be made to some of the works already mentioned, and also to Moeller's studies on the Forensic Importance of the Feces.[1]

[1]Wiener klin. Rundschau, 1897, No. 11. The standard Atlases of Pharmacognosy, Tschirch and Oerstele, Moeller, Koch, etc., are invaluable as reference works in this type of research. Jelliffe, Introduction to Pharmacognosy, 1904.

CHAPTER XVI.

BACTERIOLOGICAL EXAMINATION OF FECES.

The bacteriological examination of feces is a very recent development of laboratory diagnosis, and may truly be said to be still in its infancy. Of the bacteria which occur in feces, only a very minute proportion are capable of isolation and artificial cultivation. It is often not possible to identify certain pathogenic forms, *e. g.*, the typhoid bacillus, even when they occur in the stools in very large numbers. As is usually the case under such circumstances, the number and variety of the methods which have been elaborated is in inverse proportion to the paucity of the results. It has been deemed best, therefore, to include in the following pages only those methods and only those conclusions which seem fairly firmly established, leaving aside all discussions in the many vexed problems which have not as yet found a solution.

Methods.—It is evident that if the feces are to be subjected to bacteriological examination, pains must be taken to obtain them in an uncontaminated condition. For this purpose, only freshly passed stools should be utilized, inasmuch as the bacterial flora is very much altered by standing.

For infants, in whom the fecal matter is always soft, Escherich suggested the following device: The anus is thoroughly cleaned with some mild disinfectant, and a sterilized rod is then introduced into the rectum to irritate it; evacuations "produced under sterile precautions" are thus available at all times. Cohnheim devised a metal instrument of small caliber, carrying an eye at one end, which may be introduced into the infant's rectum, and carries away small samples in the eye. In adults, the hardness of the fecal mass defeats these measures. Here it is best simply to break open the fecal cylinder with spatulæ, and remove material for examination from the interior.

The first step in every examination of feces is the microscopical examination, either in the hanging drop, or in stained preparations, or, preferably, both. This procedure ought never to be omitted, because it offers a far truer picture of the actual conditions than can ever be obtained by cultural work. Unfortunately,

the vast majority of the fecal bacteria do not grow on the artificial media, and would, therefore, entirely escape observation were the direct microscopical examination omitted.

For hanging drop preparations, it is advisable always to dilute the fecal matter liberally with water. For stained preparations, the bacteria should be separated by centrifugation. A bit of feces half as large as a pea is rubbed up with a few cc. of water, and then centrifuged, whereby the bacteria are held in suspension, and the other material sinks to the bottom. The supernatant fluid is then diluted with twice its bulk of 95 per cent. alcohol, and again centrifuged; a sediment, which contains bacteria almost exclusively, is thus obtained. This is evenly distributed on a slide, either with an oese, or by Ehrlich's blood-smearing method, and is then stained. For routine work, the stains used are Loffler's methylen blue, or a 10 per cent. solution of carbolfuchsin.

A very useful stain, especially in certain diseases of infancy, is the Gram stain, as modified by Weigert-Escherich (1. 5 grains gentian violet in 200 cc. of water, boiled one-half hour, and filtered. 2. 11 cc. absolute alcohol mixed with 3 cc. anilin oil. 3. Lugol's solution: 1 grain iodine, 2 grains potassium iodide, 60 cc. water. 4. Anilin oil and xylol, aa. 5. Xylol).

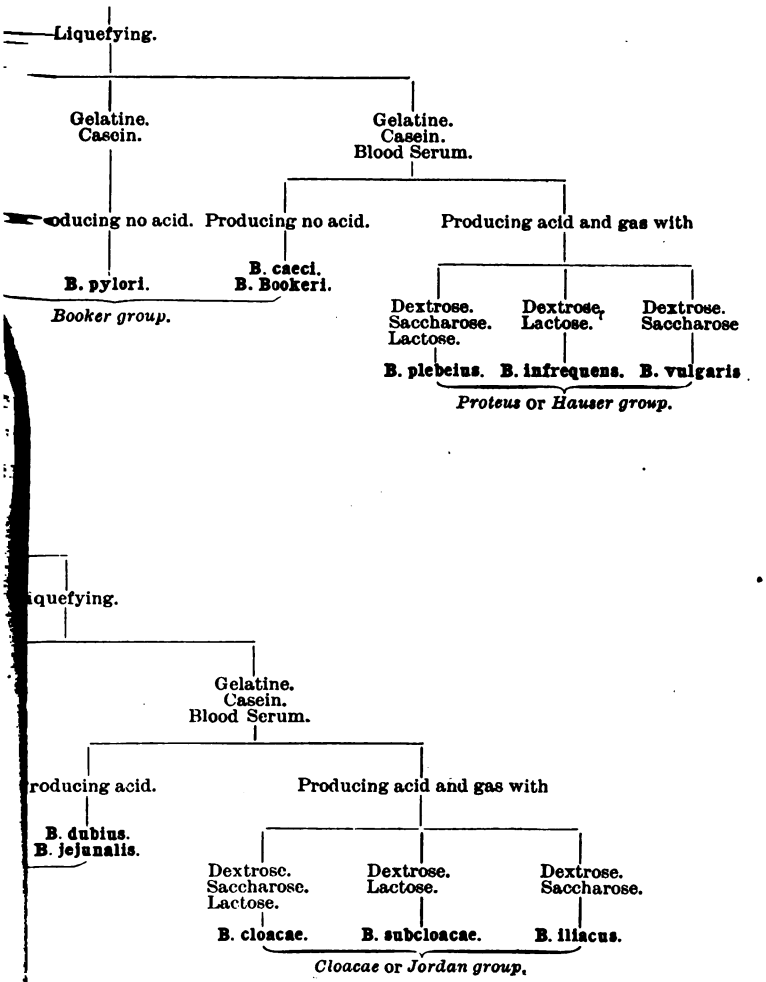
To stain: 8½ parts of 1 and 1½ of 2 are mixed, left on slide for one-half minute, and then dried with filter paper. Lugol's solution allowed to rapidly flow over slide, then blotted. The slide is now treated with anilin xylol until no more blue clouds are given off, and then washed in xylol. As a counter stain, fuchsin may be used.

For special bacteria, notably the tubercle bacillus, differential stains are in use.

Cultural methods cannot be described here in detail, but must be sought in the general bacteriological text-books. Such methods as belong particularly to coprological diagnosis, *e. g.*, the identification of typhoid germs, will be briefly described in connection with the bacteria.

Normal Stool.—The meconium is, of course, at first sterile, but begins to show the presence of bacteria generally within ten to seventeen hours after birth. The flora is very diverse, consisting of numerous forms of cocci and bacilli, all of which are derived from the air.

With the onset of the period of breast-feeding, the flora changes and becomes very characteristic. The smear contains almost exclusively long, slender bacilli, arranged often in parallel groups.



a do not include by any means all the organisms which are known to sms actually found during the progress of this investigation. A large acid to coagulate milk—is not included, inasmuch as neither *Bacillus*

i-producing liquefying bacteria, which have no action on carbohydrate up" includes bacteria which produce acid, liquefy various media and on carbohydrates other than lactose. Both these extra groups are,

ve been utilized. Not only are further combinations of carbohydrates ain cases have already been cultivated from sources outside the human Coli Group," but which is characterized by the fermentation of dextrose liquefying gelatine and casein but possessing the other features of these

resented by *Bacillus alcaligenes* of Petruschky, an organism which is characterized, as is already well known, by *non-liquefaction* of the proteids, by *failure* to *ferment* any *sugars* to the point of acidity and consequent limitation of the growth of the organism to the bulb of the fermentation tube; and by the immediate production of alkali in litmus milk.

"Next to this group stands a group of very considerable importance, and represented by *Bacillus pseudodysentericus,* the 'Dysenteric Group,' characterized by non-liquefaction of proteids, by the fermentation of carbohydrates to the point of acidity and by an initial acidity in litmus milk followed by intense alkali-production.

"This group will naturally be followed by a group embracing those organisms endowed with the capacity of splitting up carbohydrates to the point of acidity and gas production, but agreeing with the previous organisms in non-liquefaction of proteids and in an initial acidity in milk followed by alkali-production. Such organisms are included in the Hog-cholera group, embracing *Bacillus alcalescens,* fermenting dextrose, saccharose and lactose; *Bacillus subalcalescens,* fermenting dextrose and lactose; *Bacillus enteritidis,* fermenting dextrose, and *Bacterium galactophilum,* fermenting only saccharose and lactose.

"Following the same line of argument, we next have organisms which likewise ferment the carbohydrates, produce an initial acidity in litmus milk, followed by alkali-production, and which are further endowed with the capacity of liquefying the proteids. In one group liquefying gelatine alone, the 'Entericus Group,' two organisms may be distinguished, the *Bacillus entericus,* fermenting dextrose, saccharose and lactose, and *Bacillus subentericus,* breaking up dextrose and lactose. In another group, liquefying gelatine, casein and blood serum, the 'Proteus Group,' three members. may be made out:—1st, *Bacillus plebeius,* fermenting dextrose, saccharose and lactose; 2d, *Bacillus vulgaris,* breaking up dextrose and saccharose, and 3d, *Bacillus infrequens,* breaking up dextrose and lactose.

"Finally a last group of organisms may be made out, characterized by *non-fermentation* of *carbohydrates,* their growth being limited to the open bulb of the fermentation tube, by immediate alkali-production in litmus milk and by the liquefaction of various media. In this group, the 'Booker Group' may be distinguished *Bacillus recti,* liquefying gelatine, *Bacillus pylori,* liquefying gelatine and casein, and *Bacillus cæci* and *Bacillus Bookeri,* both liquefying gelatine, casein and blood serum.

"In the same way the various acid-producing bacteria may be arranged in certain groups differing from each other by gradations in reactions similar to those seen with the alkali-producers. In the first group, the 'Bienstock Group,' may be placed organisms which occupy a position among the acid-producers analogous to that of *Bacillus alcaligenes* among the alkali-producers, in that its two members, *Bacterium Bienstockii* and *Bacterium oxygenes*, are both characterized by the acidification and coagulation of milk, the non-liquefaction of the proteids and the failure to produce acid in carbohydrate solutions in the fermentation tube.

"Next to this group comes a group with similar properties of acidification and coagulation of milk and non-liquefaction of proteids, but one in which the fermentation of the carbohydrates to the point of acidity occurs. This group is represented by three members, *Bacterium minutissimum, Bacterium acidoformans* and *Bacillus oxyphilus.*

"Following the same sequence of characters, we next have non-liquefying organisms acidifying and coagulating milk, but fermenting the carbohydrates to acid and gas production. The four members of this group, *Bacillus coli, Bacillus communior, Bacterium ærogenes* and *Bacterium duodenalis.* These will be considered at some length. This group occupies among the acid-producers a position similar to that filled by the Hog-Cholera group among the alkali-producing bacteria."

Two groups of organisms next occur which are similar to the bacteria just mentioned in their acidification and coagulation of milk, and in their fermentation of the sugars, but which are capable of liquefying the carbohydrates. In the first group, liquefying gelatine only, *Bacillus gastricus* and *Bacillus subgastricus* have been considered already, as well as the three members of the "Cloacæ Group" which liquefy gelatine, casein and blood serum, namely, *Bacillus cloacæ, Bacillus subcloacæ* and *Bacillus iliacus.*

Finally a second series of organisms follows which includes the various cultures acidifying and coagulating milk, breaking up carbohydrates to the point of acidity and liquefying various media. This group includes *Bacterium chylogenes* and *Bacterium chymogenes,* liquefying gelatine, *Bacillus leporis,* liquefying gelatine and blood serum, and *Bacillus dubius* and *Bacillus jejunalis,* liquefying gelatine, casein and blood serum.

We thus may tabulate the various acid and alkali-producing bacteria of the human intestine which have been isolated, as follows:

PLATE IX.

FIG. 1.

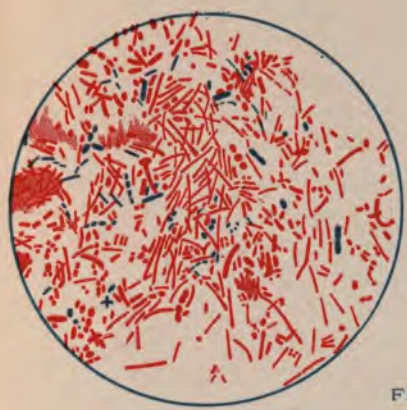


FIG. 2.

FIG. 3.

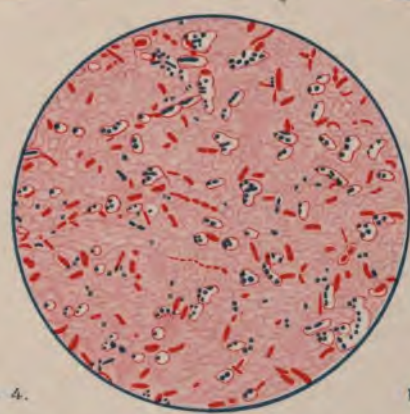


FIG. 4.

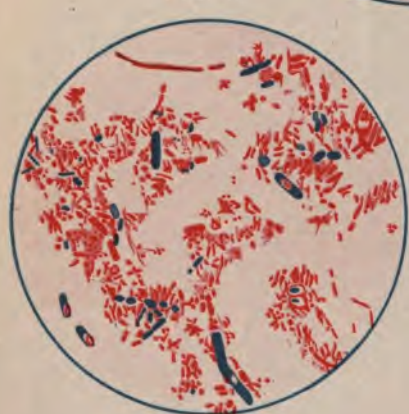


FIG. 5.

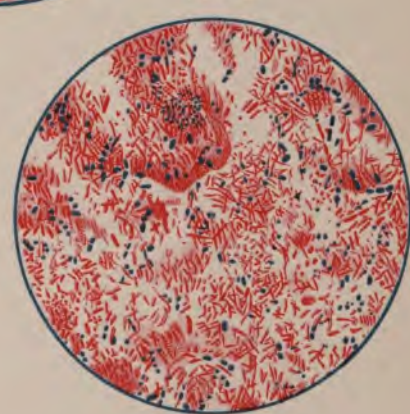


Fig. 1.—Diarrheal stools of an adult, with long, red bacilli. Weigert-Escherich stain. × 1000.

Fig. 2.—Normal stool of breast-fed infant. Smear. Stained as in Fig. 1. × 1000.

Fig. 3.—Normal stool of bottle-fed infant. Details as in Fig. 1.

Fig. 4.—Normal adult stool, on a diet chiefly of carbohydrates. Centrifugation as described in text. Details as in Fig. 1.

Fig. 5.—Normal adult stool, on a predominantly meat diet. Details as in Fig. 1. From Schmidt and Strasburger.

ALKALI-PRODUCERS.

GROUP I.—Organisms producing alkali in litmus milk not liquefying any media, not fermenting carbohydrates to the point of acidity:—FÆCALIS ALCALIGENES, or PETRUSCHKY GROUP. Represented in the forms isolated by

1. *Bacillus alcaligenes,* Migula, 1900.

GROUP II.—Organisms producing alkali, not liquefying any media, fermenting carbohydrates to the point of acidity but no gas:—DYSENTERICUS or SHIGA GROUP. Represented by

2. *Bacillus dysenteriæ.*
3. *Bacillus pseudodysentericus,* Müller, 1902.
4. *Bacillus typhi.*
5. *Bacillus acidophilus.*

GROUP III.—Organisms producing alkali, not liquefying any media, fermenting the carbohydrates with the production of acidity and gas:—HOG-CHOLERA or SUIPESTIFER GROUP. Represented by

6. *Bacillus alcalescens,* Ford, 1903—Fermenting dextrose, saccharose and lactose.
7. *Bacillus subalcalescens,* Ford, 1903—Fermenting dextrose and lactose.
8. *Bacillus enteritidis,* Gärtner, 1888—Fermenting dextrose.
9. *Bacterium galactophilum,* Ford, 1903—Fermenting saccharose and lactose.

GROUP IV.—Organisms producing alkali, liquefying gelatine, fermenting carbohydrates with the production of acid and gas:—ENTERICUS GROUP. Represented by

10. *Bacillus entericus,* Ford, 1903—Fermenting dextrose, saccharose and lactose.
11. *Bacillus subentericus,* Ford, 1903—Fermenting dextrose and lactose.

GROUP V.—Organisms producing alkali, liquefying gelatine, casein and blood serum, fermenting carbohydrates with the production of acid and gas:—PROTEUS or HAUSER GROUP. Represented by

12. *Bacillus plebeius,* Ford, 1903—Fermenting dextrose, saccharose and lactose.
13. *Bacillus infrequens,* Ford, 1903—Fermenting dextrose and lactose.
14. *Bacillus vulgaris,* (Hauser, 1885) Migula, 1900—Fermenting dextrose and saccharose.

GROUP VI.—Organisms producing alkali, liquefying various media, but not fermenting carbohydrates to the point of acidity:—BOOKER GROUP. Represented by

15. *Bacillus recti,* Ford, 1903—Liquefying gelatine.
16. *Bacillus pylori,* Ford, 1903—Liquefying gelatine and casein.
17. *Bacillus cæci,* Ford, 1903—Liquefying gelatine, casein and blood serum.
18. *Bacillus Bookeri,* Ford, 1903—Liquefying gelatine, casein and blood serum.
19. *Bacillus pyocyaneus.*

ACID-PRODUCERS.

GROUP I.—Organisms acidifying and coagulating milk, not liquefying any media, not fermenting carbohydrates to the point of acidity:—FÆCALIS OXYGENES OR BIENSTOCK GROUP. Represented by

20. *Bacterium oxygenes,* Ford, 1903.
21. *Bacterium Bienstockii,* Schröter, 1886.

GROUP II.—Organisms acidifying and coagulating milk, not liquefying any media, fermenting carbohydrates to the point of acidity but no gas:—ACIDOFORMANS OR STERNBERG GROUP. Represented by

22. *Bacillus oxyphilus,* Ford, 1903.
23. *Bacterium acidoformans,* Sternberg, 1892.
24. *Bacterium minutissimum,* Migula, 1900.

GROUP III.—Organisms acidifying and coagulating milk, not liquefying any media, fermenting carbohydrates with the production of acidity and gas:—COLI OR ESCHERICH GROUP. Represented by

25. *Bacillus coli,* Migula, 1900—Fermenting dextrose and lactose.
26. *Bacillus communior,* Ford, 1903—Fermenting dextrose, saccharose and lactose.
27. *Bacterium aërogenes,* Migula, 1900—Fermenting dextrose, saccharose and lactose.
28. *Bacterium duodenale,* Ford, 1903—Fermenting dextrose and lactose.

GROUP IV.—Organisms acidifying and coagulating milk, liquefying gelatine and fermenting the carbohydrates with the production of acidity and gas:—LIQUEFACIENS OR EISENBERG GROUP. Represented by

29. *Bacillus gastricus,* Ford, 1903—Fermenting dextrose, saccharose and lactose.
30. *Bacillus subgastricus,* Ford, 1903—Fermenting dextrose and lactose.
31. *Bacterium liquefaciens,* (Eisenberg, 1892), Ford, 1903—Fermenting dextrose, saccharose and lactose.
32. *Bacterium subliquefaciens,* Ford, 1903—Fermenting dextrose and lactose.

GROUP V.—Organisms acidifying and coagulating milk, liquefying gelatine, casein and blood serum and fermenting the carbohydrates with the production of acidity and gas:—CLOACÆ or JORDAN GROUP. Represented by

33. *Bacillus cloacæ,* Jordan, 1896—Fermenting dextrose, saccharose and lactose.
34. *Bacillus subcloacæ,* Ford, 1903—Fermenting dextrose and lactose.
35. *Bacillus iliacus,* Ford, 1903—Fermenting dextrose and saccharose.

GROUP VI.—Organisms acidifying and coagulating milk, liquefying various media, fermenting the carbohydrates with the production of acid, but no gas:—DUBIUS OR KRUSE GROUP. Represented by

36. *Bacillus chylogenes,* Ford, 1903—Liquefying gelatine.
37. *Bacterium chymogenes,* Ford, 1903—Liquefying gelatine.
38. *Bacillus leporis,* Migula, 1900—Liquifying gelatine and blood serum.
39. *Bacillus dubius,* Kruse, 1896—Liquefying gelatine, casein and blood serum.
40. *Bacillus jejunalis,* Ford, 1903—Liquefying gelatine, casein and blood serum.

The following pigment-producing and spore-bearing organisms have been isolated:

41. *Pseudomonas aëruginosa* (Schröter, 1872), Migula, 1900.
42. *Pseudomonas ovalis* (Ravenel, 1896), Chester, 1901.
43. *Bacterium Havaniense* (Sternberg, 1892), Chester, 1901.
44. *Bacterium lutescens,* Migula, 1900.
45. *Bacterium anthracoides* (Hueppe & Wood, 1881), Migula, 1900.
46. *Bacterium implectans,* Burchard, 1898.
47. *Bacillus cereus,* Frankland, 1887.
48. *Bacillus mycoides,* Flügge, 1886.

49. *Bacterium lacticola,* Migula, 1900.
50. *Bacterium vermiculare* (Frankland, 1889), Migula, 1900.
51. *Bacillus vulgatus,* Trevisan, 1889.
52. *Bacillus brevis,* Migula, 1900.
53. *Bacillus subtilis,* (Ehrenberg, 1833), Cohn, 1872.
54. *Bacillus arachnoideus,* Migula, 1900.

1. BACILLUS ALCALIGENES, Migula, 1900.

Literature and Synonyms: Bacillus fœcalis alcaligenes.—Petruschky, 1896, Bacillus fæcalis alcaligenes (n.sp). Centralblatt für Bakteriologie, Parasitenk. u. Infektionskr., Vol. XIX, p. 187 (not *Bacillus fœcalis,* Kruse, 1896).

Bacillus alcaligenes (Petruschky) Migula, 1900.—Migula, 1900, System der Bakterien, p. 737.

Bacillus alcaligenes Petruschky—Chester, 1901, Manual of Determinative Bacteriology, p. 218.

First isolated by Petruschky from typhoid stools.

Morphology.—Bacilli resembling *Bacillus typhosus* in morphology, measuring 0.5 by 1-2 microns in dimensions, often growing in pairs and in long filaments made up of individual bacilli.

Motility.—Actively motile, especially in old cultures.

Spores.—Not formed.

Agar Slant.—White, glistening growth limited to line of inoculation, not spreading nor sloping.

Agar Colonies.—Deep colonies, round, uniform, opaque; superficial colonies, usually transparent, circumscribed, but may spread slightly, showing opaque centers and slightly thinner edges, often assuming diverse shapes.

Broth.—Heavy thick scum on the surface, the broth itself being fairly clear and often free from sediment.

Gelatine Stab.—Abundant growth along line of inoculation. *No liquefaction.*

Gelatine Colonies.—Deep colonies, round and regular; superficial colonies, round, translucent, with nail-form appearance.

Potato.—Growth varies from a scanty white to an abundant dirty-yellowish or brownish mass covering entire surface of potato. Growth rarely reddish brown.

Fermentation Tube: Dextrose Broth.—Growth limited to open bulb where a thick, heavy scum is formed on the surface, and a heavy sediment settles down to the branch. *Reaction* in bulb, *alkaline.* No growth in closed arm.

Saccharose and *Lactose* not fermented to acid or acid and gas.

Blood Serum.—Abundant white or yellowish brown growth along line of inoculation. *No liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Produced rarely in old cultures.

Fecal Odor.—Rare, may appear in old cultures.

Litmus Milk: Characteristic Reaction.—Production of alkali immediate; within forty-eight hours milk turns blue; no stage of preliminary acidity; alkali-production continues for some days. *No coagulation* of the milk. After neutralization of the alkali with weak acid the casein is found undissolved.

Pathogenicity.—Non-pathogenic to mice, guinea-pigs or rabbits.

Occurrence and Distribution.—Found in fourteen cases of fifty examined. Found in rectum alone in five cases, in cecum alone in two cases, in duodenum alone in three cases. Found in combination, in rectum and stomach, in rectum and duodenum, in cecum and duodenum and in duodenum and stomach. It is thus seen to be commonly present in the lower portions of the intestinal tract, more rarely appearing in the upper part of the bowel.

2. BACILLUS DYSENTERIÆ, Shiga, 1898.

Literature.—K. Shiga. Centralblatt für Bakteriologie, Parasitenkunde, und Infectionskrankheiten, 1898, Vol. XXIV.

Strong and Musgrave. Preliminary Note regarding the Etiology of the Dysenteries of Manila. Report of the Surgeon-General of the Army, Washington, 1900, p. 251.

S. Flexner. On the Etiology of Tropical Dysentery. Bulletin Johns Hopkins Hospital. 1900, p. 231.

Vedder and Duval. The Etiology of Acute Dysentery in the United States. Journal of Experimental Medicine, Vol. VI, p. 181.

In all characters, *Bacillus dysenteriæ* resembles form No. 3. It differs, however, in the serum reaction, inasmuch as it does agglutinate with immune serum.

3. BACILLUS PSEUDODYSENTERICUS, Müller, 1902.

Literature.—Kruse, 1901, Weitere Untersuchungen über die Ruhr und die Ruhrbacillen, Deutsche med. Wochenschrift, Nos. 23 and 24.

Ford, W. W., 1901, Classification of Intestinal Bacteria, Journ. of Medical Research, Vol. I, p. 211.

Müller, Paul Theodore, 1902, Ueber den bakteriologischen Befund bei einer Dysenterieepidemie in Sudsteiermark, Centralblatt für Bakteriologie, Vol. XXXI, No. 12, p. 558.

First isolated by Kruse in "Pseudodysenterie" and by Ford from normal intestinal contents.

Morphology.—Bacilli measuring 0.5 by 1-2 microns in dimensions, growing in pairs and in short chains.

Motility.—Slowly motile in young agar and broth cultures, motility more marked in old cultures.

Spores.—Not formed.

Agar Slant.—White, glistening growth along line of inoculation; no tendency to spread or slope.

Agar Colonies.—Deep colonies, round, regular and opaque; superficial colonies may be round, regular, finely granular, translucent, with clean-cut margins, or present dark centers with slightly spreading periphery. The latter may spread over the surface of the agar, assuming various bizarre shapes. The formation and appearance of particular colonies cannot be associated with particular cultures, as transfers from one variety of colonies will later originate other varieties. The regular non-spreading colonies resemble those of *Bacillus typhosus.*

Broth.—Luxuriant growth with the production of a heavy sediment; *no pellicle.*

Gelatine Stab.—Abundant growth along line of inoculation, spreading slightly on the surface of the gelatine; *no liquefaction.*

Gelatine Colonies.—Deep colonies round, regular and opaque; superficial colonies translucent, finely granular, spreading like those of *Bacillus typhosus.*

Potato.—Luxuriant yellowish brown or brown growth.

Fermentation Tube: Dextrose Broth.—Characteristic reaction. Abundant growth in bulb with a thick sediment settling down to the branch. *No pellicle. Reaction Acid.* Growth extends into closed arm where the broth speedily becomes turbid. *Reaction* of closed arm *acid;* no production of gas.

Saccharose and *Lactose* not broken up with the production of acid or gas.

Blood Serum.—Abundant white or yellowish-white growth, *no liquefaction.*

Growth never becomes red.

Nitrates.—Reduced to nitrites.

Indol.—Produced rarely in small quantities.

Fecal Odor.—Not produced.

Litmus Milk.—Characteristic reaction. Transient acidity produced within first twenty-four hours, yielding to a continuous alkali-production which turns the litmus milk blue. *No coagulation* of the milk. Neutralization shows undissolved casein.

Pathogenicity.—Mice, guinea-pigs and rabbits die after subcutaneous inoculation within twenty-four to forty-eight hours of a septicemia. Bacilli in pure culture may be obtained from the internal organs.

Occurrence and Distribution.—Found in ten different cases. Present in rectum in four cases, in cecum in one, and in stomach in one. Found in combination in four cases, in rectum and cecum twice, in cecum and duodenum and in cecum, duodenum and stomach. It is thus seen to be present especially in the lower portions of the bowel, but also to appear in the stomach as well.

Serum Reactions.—Does not agglutinate with the blood serum of patients suffering from dysentery.

4. BACILLUS TYPHI, Eberth.

Literature and Synonyms: Bacillus typhosus.—Kruse, Flügge. Lösener, Arbeiten aus dem kaiserlichen Gesundheitsamt, Berlin, 1885, contains a full bibliography of 689 titles.

Morphology.—In the organs generally short, thick bacilli (1.0-32 microns long, 0.6-0.8 broad), rarely short threads. In cultures, all varieties from short bacilli to long threads.

Motility.—The bacilli and the threads are both actively motile. Flagella 8-14.

Spores.—Not formed. Polar bodies once regarded as spores do not belong in this category.

Agar Slant.—Fairly broad growth, whitish, gray, glistening, surface apparently perforated in places, sharp margins. Water of condensation clear, little sediment.

Agar Stab.—Thread-like, at times somewhat granular, gray. Surface irregularly rounded, margins regular, grayish, then yellowish, glistening.

Broth.—Turbid, moderate sediment, which becomes homogeneously distributed on shaking.

Gelatine Stab.—Growth along line of inoculation, slightly granular. Surface growth thin, white, grayish green, opalescent, transparent, rounded irregular margins, very slightly elevated.

Gelatine plates.—Superficial colonies, at first small, yellowish, pin-point in size, soon growing larger, rounded, with irregular margins, marginal zone lighter, transparent, grayish, while the center becomes whitish and opaque. Deeper colonies, rounded or yellowish.

Potato.—Extremely delicate, moist, often almost invisible pellicle, which covers almost the entire surface of the potato. The growth to be typical should be on potatoes presenting an acid reaction.

Fermentation Tube.—Growth abundant, sediment, reaction acid, no gas.

Dextrose Broth.—Lactose broth, similar reaction.

Blood Serum.—Fairly abundant, grayish-white growth, no liquefaction.

Nitrates.—Reduced to nitrites.

Indol.—Not formed.

Fecal Odor.—Not produced.

Litmus Milk.—No coagulation, very small amount of acid produced.

Pathogenicity.—Laboratory animals die after large doses of a septicemia; similar symptoms produced by filtered cultures. Gradually increased doses produce immunity, with agglutination reaction in serum. Chantemesse and Widal have succeeded in growing a type which produces true typhoid, clinically and pathologically, in rabbits and apes.

Serum Reactions.—Agglutinates in most cases with serum in dilutions of 20-100 of patients.

5. BACILLUS ACIDOPHILUS, Moro, 1900.

Literature.—Moro, Ein Beitrag zur Kenntniss der normalen Darmbacterien des Säuglings. Jahrbuch für Kinderheilkunde, Vol. LII. Also, Ueber die nach Gram färbbaren Bacillen des Saüglingstuhles, Wiener klinische Wochenschrift, 1900, No. 5.

Morphology.—Rods measuring 1.5-2 micra in length, 0.6-0.9 micra in breadth. Extremities slightly tapering, and somewhat rounded. Occur irregularly, or in parallel groups.

Staining Reactions.—Gram positive.
Motility.—Non-motile.
Agar Slant.—Very poor growth.
Potato.—No growth.
Fermentation Tube.—Acidity, but no gas.
Other Media.—Grows best on beer-wort bouillon, and in bouillon when acidified with acetic acid or a mineral acid, so that 10 cc. are neutralized by 1 cc. of normal soda.
Occurrence.—In the stools of breast infants.

6. BACILLUS ALCALESCENS, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.
First isolated from intestinal contents and described by Ford.
Morphology.—Bacilli measuring 0.5 by 1 to 2 microns, usually appearing as single individuals, but occasionally growing in long chains.
Motility.—Actively motile.
Spores.—Not formed.
Agar Slant.—White translucent growth, either limited to line of inoculation or spreading rapidly from this line within forty-eight hours, covering the whole agar slant and sloping to the bottom of the tube.
Agar Colonies.—Deep colonies round, regular, opaque; superficial colonies have opaque white centers with spreading translucent periphery.
Broth.—Turbidity and sediment, no formation of pellicle.
Gelatine Stab.—Abundant growth along line of inoculation, and on the surface of the gelatine. *No liquefaction.*
Gelatine Colonies.—Deep colonies, round, regular; superficial colonies have dark opaque centers and spreading peripheries.
Potato.—Growth varies from a scanty yellowish-white to an abundant dirty-brown mass.
Fermentation Tube: Dextrose Broth.—Abundant growth in bulb with the formation of a heavy sediment. *Reaction* in bulb, *acid.* Growth in closed arm with the evolution of *gas* and the production of *acidity.*
Saccharose and *Lactose* also fermented with the production *of acid and gas.*
Blood Serum.—Abundant opaque white growth. *No liquefaction.*
Nitrates.—Reduced to nitrites.

Indol.—Rarely produced.

Fecal Odor.—Rarely produced.

Litmus Milk.—Preliminary acidity yielding in forty-eight hours to an intense alkali-production: *no coagulation* of the milk; *no peptonization* of the casein.

7. BACILLUS SUBALCALESCENS, Ford, 1903.

Literature.—Ford, W. W., 1901. Classification of Intestinal Bacteria. Journal of Medical Research, Vol. I. p. 211.

Isolated from intestinal contents and described by Ford. This organism differs from the preceding only in its failure to ferment saccharose—dextrose and lactose alike being broken up with the production of acid and gas. In its colony formation and in its cultural features it is identical with the organism just described. Several cultures were obtained from four cases where it appeared twice in the rectum, once in the cecum and once in the duodenum.

8. BACILLUS ENTERITIDIS, Gärtner, 1888.

Literature.—Gärtner, 1888, Ueber die Fleischvergiftung in Frankenhausen am Kyffhäuser und den Erreger Desselben. Corresp. d. allg. Arztl. Vereins Thüringen No. 9.

Migula, 1900, System der Bakterien, p. 744.

Chester, 1901, Manual of Determinative Bacteriology, p. 207.

First isolated and described by Gärtner in epidemics of meat poisoning. Identical culturally with,

Bacillus paracolon, Widal, 1897, La Semaine Médicale, August 4th.

Bacillus paracolon, Gwynn, 1898, Johns Hopkins Hospital Bulletin, March, p. 54.

Bacillus O., Cushing, 1900, ibid., July, August, p. 157.

Bacillus icteroides, Sanarelli, 1897, British Medical Journal, July 3d; 1898, Centralblatt für Bakteriologie, 29, p. 376.

Bacillus paratyhpoid, Schottmüller, 1901. Zeitschrift für Hygiene, Vol. XXXVI, p. 368.

Morphology.—Bacillus measuring 0.5 by 1.5 to 2 microns, appearing either as single elements, as pairs, or as short chains.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Grayish-white growth along line of inoculation without tendency to spread or slope.

Agar Colonies.—Deep colonies, round, regular, uniform and opaque; superficial colonies, round, translucent, with dark nucleus—not spreading.

Broth.—Turbidity, no scum.

Gelatine Stab.—Abundant growth, *no liquefaction.*

Gelatine Colonies.—Deep colonies regular brown, superficial colonies, round, gray, translucent, granular.

Potato.—Abundant brown or yellowish-brown growth.

Fermentation Tube: Dextrose Broth.—Abundant growth in bulb with heavy sediment; *reaction acid.* Growth in closed arm, abundant evolution of gas; reaction of closed arm *acid.*

Saccharose and *Lactose* not fermented.

Blood Serum.—Abundant dirty-white growth; *no liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Preliminary acidity yielding to alkali-production within forty-eight hours; *no coagulation.* No peptonization of casein.

9. BACTERIUM GALACTOPHILUM, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First isolated from intestinal tract and described by Ford.

Morphology.—Bacteria measuring 0.75 by 1.5 microns, appearing in single elements.

Motility.—Non-motile.

Spores.—Not formed.

Agar Slant.—Raised, viscid, sweaty growth, spreading along line of inoculation, but not sloping to bottom of tube. When touched with platinum needle long threads are brought away.

Agar Colonies.—Colonies vary in size, are usually round, project from the surface, are dull-white in color, appearing not unlike drops of sweat.

Broth.—Turbidity, scum on the surface and an abundant sediment.

Gelatine Stab.—Abundant growth, *no liquefaction.*

Gelatine Colonies.—Deep colonies, round and regular; superficial colonies irregular, skein-like with spreading processes.

Potato.—Abundant dull white growth.

Fermentation Tube: Dextrose Broth.—Thick scum and heavy sed-

iment in bulb, no growth in closed arm; *reaction* in bulb ***alkaline.*** Dextrose not broken up.

Saccharose and *Lactose* both fermented with the production of *acid* and *gas.*

Blood Serum.—Abundant white growth, *no liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Preliminary acidity followed by intense alkali-production. No coagulation. No peptonization of the casein.

10. BACILLUS ENTERICUS, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First isolated from intestinal contents and described by Ford.

Morphology.—Bacilli measuring 0.5 by 1.5-3.0 microns, often growing out into long chains.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—White, glistening growth, spreading over the surface of agar, and when specially luxuriant sloping to the bottom of the tube, where it forms a thick, heavy mass.

Agar Colonies.—Deep colonies, round, regular, opaque; superficial colonies have white opaque centers and slightly-spreading peripheries. Colonies never spread as much as those of *Bacillus vulgaris,* and are easily distinguished from them.

Broth.—Marked turbidity, no scum.

Gelatine.—Rapid *liquefaction* from surface downward; within twenty-four hours a thick rim of liquefied gelatine is produced and by the end of the fifth day the entire mass of gelatine is transformed to a thin fluid.

Gelatine Colonies.—Small, round, regular, translucent colonies, often in rouleaux and giving a "broken glass" appearance.

Potato.—Luxuriant dirty-brown growth spreading rapidly over the surface of the potato.

Fermentation Tube: Dextrose Broth.—Turbidity in bulb; heavy sediment; *acid reaction; growth* in *closed arm; acid reaction* and evolution of *gas.*

Saccharose and *Lactose* also split up into *acid* and *gas.*

Blood Serum.—Thick white growth, *no liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Produced, often in large quantity.

Fecal Odor.—Rarely produced.

Litmus Milk.—Preliminary acidity followed by intense alkali-production. *No liquefaction.* Upon neutralization casein found undissolved.

11. BACILLUS SUBENTERICUS. Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

Organism similar to *Bacillus entericus* in the majority of their reactions, but failing to ferment saccharose were isolated in two cases. They represent a sub-species of this micro-organism. They were present in the stomach of one case and in the cecum of another.

12. BACILLUS PLEBEIUS, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

Morphology.—Bacilli 0.5 by 1.5-3.0 microns appearing in pairs or in long chains.

Motility.—Actively motile, especially in old cultures.

Spores.—Not formed.

Agar Slant.—White glistening abundant layer spreading over the surface of agar and sloping to bottom of tube.

Agar Colonies.—Deep colonies round or oval, brown in color; superficial colonies have opaque white centers and spreading translucent peripheries with frequent branching threads. Colonies may assume various bizarre shapes.

Broth.—Marked turbidity. Rarely the production of a delicate film on the surface.

Gelatine.—Abundant growth along line of inoculation; rapid and complete *liquefaction* of gelatine beginning at the surface and proceeding downward.

Gelatine Colonies.—Spreading colonies with dark opaque centers and lighter periphery. Rapid *liquefaction* about the individual colonies.

Potato.—Abundant yellowish-white or creamy-white growth turning brown or red in old cultures.

Fermentation Tube: Dextrose Broth.—Marked turbidity and sediment in open bulb; rapid growth in closed arm with production of a large quantity of *gas. Reaction in bulb* and *closed arm acid.*

Gas and acid also from *Saccharose* and *Lactose.*

Blood Serum.—Abundant growth; slow but complete *liquefaction.*
Nitrates.—Reduced to nitrites.
Indol.—Rarely produced.
Fecal Odor.—Not produced. Odor of putrefaction common to this group.
Litmus Milk.—Preliminary acidity followed by intense alkali-production. No coagulation of the milk. Slow digestion of the casein which, after eight to ten days, is completely dissolved. Reduction of the litmus takes place at the same time, the resulting fluid being clear, transparent, soapy, with small drops of oil floating on the surface. Neutralization shows the complete *peptonization* of the casein.

13. BACILLUS INFREQUENS, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

Organisms differing from the preceding form in their failing to ferment saccharose, but agreeing with it in their main cultural features may conveniently be grouped together under the name *Bacillus infrequens.*

This form was obtained by Ford in nine cases, in rectum once, in cecum once, in duodenum three times and in combination in rectum and cecum once, in rectum and stomach twice, and in duodenum and stomach once. It is thus more frequently met with in the upper portions of the alimentary canal, being especially common to the duodenum.

14. BACILLUS VULGARIS (Hauser, 1885), Migula, 1900.

Literature and Synonyms: Proteus vulgaris.—Hauser, 1885, Ueber Faulniss-bacterien, Leipzig.

Bacillus proteus.—Trevisan, 1889, Genera.

Bacillus vulgaris.—(Hauser) Migula, 1900, System der Bakterien, p. 707.

Bacillus vulgaris (Hauser), Chester, 1900, Manual of Determinative Bacteriology, p. 244.

First isolated from putrefying masses by Hauser.

Morphology.—Bacilli 0.5-1.0 by 1.0-3.0 microns in dimensions, appearing in pairs, but frequently in long chains. Great diversity in morphological appearance, the individual elements frequently looking like micrococci, or very stumpy bacilli.

Motility.—Young cultures show sluggish motility, old cultures often show active motility.

Spores.—Not formed.

Agar Slant.—Thin bluish-gray growth, spreading rapidly over the surface of the agar and sloping to the bottom of the tube.

Agar Colonies.—Typical spreading colonies with opaque white centers and outlying bluish-gray periphery. Deep colonies, round or oval, brown in color.

Broth.—Turbidity marked, rarely a scum.

Gelatine.—Abundant growth; rapid and complete *liquefaction,* beginning at the surface and extending downwards along line of inoculation.

Gelatine Colonies.—Irregular spreading colonies with rapid *liquefaction* of the gelatine about them.

Potato.—Abundantly yellowish-white, or creamy-white growth, turning brown in old cultures.

Fermentation Tube: Dextrose Broth.—Rapid growth with production of a heavy sediment. Growth in closed arm. *Abundant gas. Acid reaction* in bulb and branch.

Saccharose broken up into *acid* and *gas.*

Lactose not affected by this bacillus.

Blood Serum.—Abundant growth. *Slow and complete liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced. Putrefactive odor common.

Litmus Milk.—Preliminary acidity followed by intense alkali-production with *peptonization* of the casein and reduction of the litmus. Usually a soft coagulum is produced. After ten days milk transformed to a thin, colorless liquid with a few oil drops floating on the surface.

15. BACILLUS RECTI, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First obtained from intestinal contents and described by Ford.

Morphology.—Bacilli measuring 0.5 by 1.5-2.0 microns, occurring usually in pairs and chains.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Grayish-white growth limited to line of inoculation, not spreading or sloping.

Agar Colonies.—Deep colonies, round, regular, uniform; superficial colonies very large, have opaque centers and very slightly spreading edges without branching.

Broth.—Turbidity; no scum.

Gelatine.—Rapid and complete *liquefaction* along line of inoculation.

Gelatine Colonies.—Round or oval colonies, brown in color with great variations in size and shape.

Potato.—Luxuriant brownish-red growth.

Fermentation Tube: Dextrose Broth.—Turbidity in open bulb to which the growth is limited; no growth in closed arm. *Reaction* of bulb *alkaline.*

Saccharose and *Lactose* not fermented.

Blood Serum.—Abundant white glistening growth *without liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—No preliminary acidity. Immediate alkali-production. No *coagulation* of the milk. No *peptonization* of the casein.

16. BACILLUS PYLORI, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First obtained from intestinal contents by Ford.

Morphology.—Large bacilli measuring 1.0 by 3.0-4.0 microns, never appearing in chains.

Motility.—Very actively motile. Bacilli shoot rapidly from one portion of the field to another with the velocity of a cholera vibrio.

Spores.—Not formed.

Agar Slant.—Spreading white translucent growth.

Agar Colonies.—Deep colonies round and regular; superficial colonies spread over the surface with opaque white centers and outlying edges.

Broth.—Turbidity, no scum.

Gelatine Stab.—Abundant growth. *Rapid liquefaction* from surface downward.

Gelatine Colonies.—Deep colonies round and regular; superficial colonies grayish with dark opaque centers and outlying translucent ring not spreading.

Potato.—Luxuriant dull white growth.

Fermentation Tube: Dextrose Broth.—Growth limited to open bulb where a heavy sediment is produced. No growth in closed arm. *Reaction* of *bulb alkaline.*

Saccharose and *Lactose* not broken up.

Blood Serum.—Abundant white growth, *no liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Preliminary acidity followed by alkali-production. *No coagulation* of the milk. *Rapid peptonization* of the *casein* and *reduction* of the *litmus.*

17. BACILLUS CÆCI, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First obtained from intestinal contents by Ford.

Morphology.—Long thick bacilli measuring 0.75 by 2.0-.4.0 microns, usually growing in long chains.

Motility.—Very sluggishly motile.

Spores.—Not formed.

Agar Slant.—Brown sweaty growth along line of inoculation without spreading or sloping.

Agar Colonies.—Opaque, round, non-spreading colonies.

Broth.—Turbidity and rarely the production of a scum.

Gelatine Stab.—Abundant growth along line of inoculation. Rapid and complete *liquefaction.*

Gelatine Colonies.—Irregular brown colonies, often associated in long rouleaux and cork-screws.

Potato.—Luxuriant yellowish-white growth.

Fermentation Tube: Dextrose Broth.—Growth limited to open bulb where a great turbidity is produced. No growth in closed arm; *reaction alkaline.*

Saccharose and *Lactose* not broken up.

Blood Serum.—Abundant yellowish-white growth and a slow but complete liquefaction.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—No preliminary acidity. Intense alkali production. No coagulation. Rapid liquefaction of casein.

18. BACILLUS BOOKERI, Ford, 1903.

Literature and Synonym.—*Bacillus A.* Booker. Sternberg, 1896, Manual of Bacteriology, p. 492.

First isolated from alvine discharges of children suffering with cholera infantum, by Booker.

Morphology.—Small bacilli measuring ½ x 1½ to 2 mikrons.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Abundant yellowish or yellowish-brown growth along line of inoculation, not spreading or sloping.

Agar Colonies.—Deep colonies, round, regular, opaque; superficial colonies have opaque centers and transparent thin film in periphery, which gradually merges with surrounding agar, giving an indistinct bluish look.

Broth.—Marked turbidity, no scum.

Gelatine.—Abundant growth along line of inoculation; slow but complete liquefaction along line of puncture.

Gelatine Colonies.—Round brown colonies of various sizes.

Potato.—Luxuriant yellowish-white growth.

Fermentation Tube: Dextrose Broth.—Abundant growth in open bulb, with the production of a heavy sediment. *No growth in closed arm. Alkaline reaction in bulb.*

Saccharose and *Lactose* also not broken up.

Blood Serum.—Yellowish-brown growth. Gradual liquefaction.

Nitrates.—Not reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—No preliminary acidity. Intense alkali-production. No coagulation. Slow and complete *liquefaction* of the casein with reduction of the litmus.

19. BACILLUS PYOCYANEUS.

Morphology.—Small bacilli measuring 1-2 by 0.3-0.5 micra. Usually single, sometimes in short chains.

Motility.—Actively motile, monotrichous.

Spores.—Absent.

Agar Slant.—Rich, moist growth.

Gelatine.—Colonies of irregularly-rounded contour, yellowish-green; liquefied.

Broth.—Clouded.

Potato.—Dry growth.

Milk.—Coagulated and peptonized in forty-eight hours.
Fermentation Tube.—Acidified, no gas.
Indol.—Produced by some colonies.
Pathogenicity.—Pathogenic for rabbits and guinea pigs.
Chromogenesis.—Pyocyanin and a yellowish-green pigment.

20. BACTERIUM OXYGENES, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.
First isolated from intestinal contents by Ford.
Morphology.—Bacteria measuring 0.5 by 2.0-3.0 microns.
Motility.—Non-motile.
Spores.—Not formed.
Agar Slant.—Thick white glistening growth, limited to line of inoculation.
Agar Colonies.—Deep colonies small, brown and regular; superficial colonies large, round, translucent, spreading over the surface of the agar and assuming a bluish look.
Broth.—Turbidity, no scum.
Gelatine Stab.—Growth along line of inoculation, *no liquefaction.*
Gelatine Colonies.—Irregular brownish colonies of various sizes and shapes, usually round or oval, not characteristic.
Potato.—Very abundant yellowish-white or yellowish-brown growth, rapidly covering cut surface of potato.
Fermentation Tube: Dextrose Broth.—Abundant growth in bulb with production of a turbidity and sediment. *Reaction alkaline. No growth in closed arm.*
Saccharose and *Lactose* not fermented.
Blood Serum.—Abundant white growth *without liquefaction.*
Nitrates.—Not reduced to nitrites.
Indol.—Not produced.
Fecal Odor.—Not produced.
Litmus Milk.—Intense acid-production. Coagulation of the milk to a dense hard mass. *No liquefaction of the casein.*

21. BACTERIUM BIENSTOCKII, Schröter, 1886.

Literature and Synonyms.—Bacillus aus Feces, No. iii, Bienstock. Bienstock, Ueber die Bakterien der Feces, Zeitschrift für klin. Med., Bd. VIII, Heft 1.
Bacterium Bienstockii, Schröter.
Schröter, 1886, Pilze Schlesien, p. 163.

Bacillus coprogenes parvus, Bienstock. Flügge, 1886, Die Mikroorganismen, 2d edition, p. 269; 1896, 3d edition, Vol. II, p. 423.

Bacterium Bienstockii, Schröter. Migula, 1900, System der Bakterien, p. 393.

Bacterium Bienstockii, Schröter. Chester, 1901, Manual of Determinative Bacteriology, p. 144.

First obtained by Bienstock from human feces.

Morphology.—Very short fine bacteria measuring 0.5 by 0.75 microns, in stained preparations barely to be distinguished from micrococci.

Motility.—Non-motile.

Spores.—Not formed.

Agar Slant.—Growth very slow; after forty-eight to seventy-two hours only a faint film produced on agar.

Agar Colonies.—Small, fine, brown, non-spreading colonies.

Broth.—Turbidity, no scum.

Gelatine Stab.—Slow growth along line of inoculation. *No liquefaction.*

Gelatine Colonies.—Small, fine regular pale brown colonies.

Potato.—Hardly perceptible, grayish-white growth.

Fermentation Tube: Dextrose Broth.—Growth in bulb, where faint turbidity is produced. *Reaction alkaline. No growth* in *closed arm.*

Saccharose and *Lactose* not fermented.

Blood Serum.—Faint white film, *no liquefaction.*

Nitrates.—Not reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Acid-production, slow coagulation, eventual production of a dense firm mass. *No liquefaction of the casein.*

22. BACILLUS OXYPHILUS, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

Isolated from intestinal contents by Ford.

Morphology.—Bacilli measuring 0.75 by 2.0 microns.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Abundant thick white growth.

Agar Colonies.—Deep colonies round, regular and grayish; superficial colonies usually have opaque white centers and slightly radiating branches.

Broth.—Turbidity and rarely a slight scum.

Gelatine Stab.—Growth along line of inoculation. *No liquefaction.*

Gelatine Colonies.—Irregular, round or oval colonies, presenting "broken glass" appearance.

Potato.—Luxuriant brownish growth.

Fermentation Tube: Dextrose Broth.—Growth in open bulb with the production of turbidity and sediment. *Reaction acid.* Growth in closed arm. *Reaction acid. No gas.*

Saccharose and *Lactose* not fermented.

Blood Serum.—Luxuriant grayish-white growth. *No liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Acid-production and coagulation of the milk within twenty-four hours. *No peptonization of the casein.*

23. BACTERIUM ACIDOFORMANS, Sternberg, 1892.

Literature and Synonyms: Bacillus acidoformans.—Sternberg, 1892, Manual of Bacteriology, p. 499.

Bact. Acidoformans, Sternberg.—Chester, 1901, Manual of Determinative Bacteriology, p. 150.

Isolated from the liver of a yellow fever cadaver by Sternberg.

Morphology.—Thick stumpy bacilli measuring 0.75 by 1.0-1.5 microns, often associated in long chains.

Motility.—Non-motile.

Spores.—Not formed.

Agar Slant.—Abundant thick white growth spreading over the surface of agar and turning brown in old cultures.

Agar Colonies.—Deep colonies, minute and brownish; superficial colonies large, opaque and circumscribed.

Broth.—Turbidity, without scum.

Gelatine Stab.—Growth along line of inoculation. *No liquefaction.*

Gelatine Colonies.—Deep colonies, fine, opaque; superficial, irregular, translucent, non-spreading.

Potato.—Luxuriant yellowish-white or yellowish-brown growth.

Fermentation Tube: Dextrose Broth.—Abundant growth in bulb with the production of a turbidity and sediment. *Reaction acid.* Abundant growth in closed arm. *Reaction acid. No gas formed.*

Saccharose and *Lactose* not fermented.

Blood Serum.—Heavy white growth *without liquefaction.*

Nitrates.—Not reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Acid reaction within twenty-four hours. Coagulation of the milk to a hard firm mass. *No peptonization of the casein.*

24. BACTERIUM MINUTISSIMUM, Migula, 1900.

Literature and Synonyms: Bacillus pyogenes minutissimus, Kruse.—Flügge, Mikroorganismen, 1896, Bd. II, p. 447.

Bacterium minutissimum, Migula, 1900. Migula, 1900, System der Bacterien, p. 418.

Isolated by Kruse from a brain abscess.

Morphology.—Fine short bacilli measuring ½ by 1 micron, appearing usually as diplo-bacilli which when stained look like diplococci.

Motility.—Non-motile.

Spores.—Not formed.

Agar Slant.—Faint transparent film visible on the surface only in twenty-four-hour cultures, after forty-eight hours sinking into the depths of the medium and distinguished with difficulty.

Agar Colonies.—Deep colonies not characteristic; superficial colonies pale gray, round or oval, appearing only after forty-eight hours.

Broth.—Slow growth, with the production of a turbidity but no scum.

Gelatine Stab.—Faint slow growth along line of puncture. *No liquefaction.*

Gelatine Colonies.—Small, round, regular, pale-brown or pale-yellow colonies.

Potato.—Faint, white, glistening growth, developing after several days.

Fermentation Tube: Dextrose Broth.—Faint turbidity in bulb with scanty sediment. *Reaction acid.* Slow growth in closed arm. *Reaction acid, no gas.*

Saccharose and *Lactose* not fermented.

PLATE X.

FIG. 1.

FIG. 2.

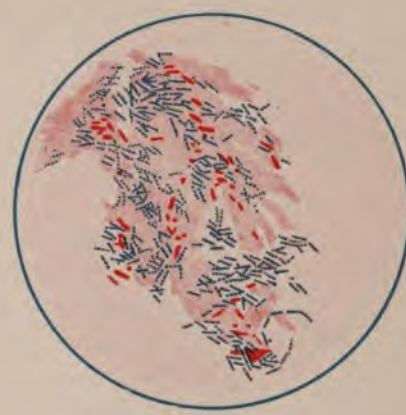


FIG. 3.

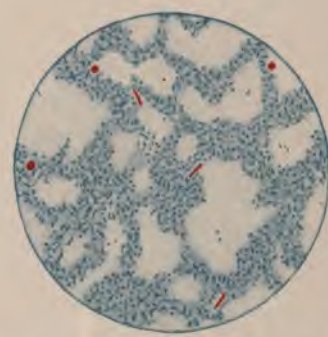


FIG. 4.

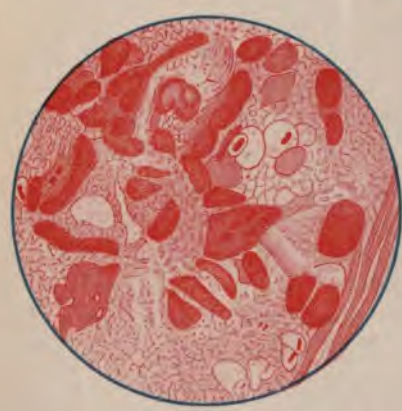


FIG. 5.

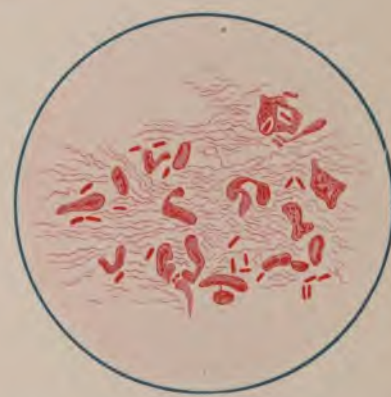


Fig. 1.—Threads of mucus from an infant's stool, in streptococcus enteritis. Stained according to Weigert-Escherich. × 1000. (After Hirsch.)

Fig. 2.—Blue bacillosis of Escherich. Details as in Fig. 1.

Fig. 3.—Tubercle bacilli from formed stools. Details as in Fig. 1. (Spores also stained red.)

Fig. 4.—Dysentery bacilli. Smear from a small clump of pus. Stained with dilute carbolic fuchsin. × 1000.

Fig. 5.—Purulent portion of an infant's stool, in a case of infectious colitis. Details as in Fig. 1.

Blood Serum.—Faint white growth. *No liquefaction.*

Nitrates—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Reaction acid. Coagulation of milk after forty-eight hours. *No peptonization of casein.*

25. BACILLUS COLI, Migula, 1900.

Literature and Synonyms: Bacterium coli commune.—Escherich, 1886, Darmbakterein des Säuglings, Stuttgart.

Neapeler Bacillus.—Emmerich, 1884, Deutsche med. Wochenschrift, No. 50.

Bacillus Neapolitanus.—Fraenkel, 1887, Grundriss der Bakterienkunde.

Emmerich's Bacillus.—Eisenberg, 1886, Bakteriologische Diagnostik.

Bacillus pyogenes-fœtidus.—Passet, 1885, Ætiologie eiterigen Phlegmon des Menschen, Berlin.

Bacillus coli. (Escherich.)—Migula, 1900, System der Bakterien, p. 734.

Bacillus coli communis verus.—Durham, 1900-1901, Journal of Experimental Medicine, Vol. V, p. 353.

Bacillus coli (Escherich).—Chester, 1901, Manual of Determinative Bacteriology, p. 205.

First isolated case by Escherich from the intestinal contents of infants.

Morphology.—Short stumpy bacilli measuring 0.5 by 1.0-2.0 microns. Occurs usually in single elements, but frequently in pairs and short or long chains. When unstained the long chains are seen to be made up of 15 to 20 separate bacilli linked together. May appear as a diplobacillus which when stained looks like a diplococcus. The diplococcoid forms are common in young cultures, or, as Adami has pointed out, are frequently seen in attenuated cultures from the tissues or from the gall bladder.

Motility.—*Bacillus coli* always possesses a well-defined motility which, while not especially active, is always sufficient to differentiate it from any bacteria. In the 200 cultures of this bacillus which were obtained at various intervals, unquestioned motility was demonstrated in every culture. The motility is usually less than that of *Bacillus typhosus* or that

of *Ps. æruginosa (Bacillus pyocyaneus)*, but occasionally cultures are encountered where the bacilli move across the field with the velocity of a *cholera vibrio*. Usually a *moderate motility*.

Spores.—At no time observed. The diplococcoid form is considered by Adami to represent an attempt on the part of the bacillus, when grown under unfavorable conditions, to assume a more resistant state, but one distinct from spore formation.

Agar Slant.—Glistening white or yellowish white growth extending rapidly along the line of inoculation, spreading and sloping to the bottom of the tube, where it develops luxuriantly. In old cultures the growth becomes dirty brown, especially after drying. Attenuated forms grow as a faint white film on the surface of agar.

Agar Colonies.—Deep colonies, round or oval, regular, sharply cut edges, slightly brown in color, nail-form growth often seen; superficial colonies are slightly opaque, brownish, either circumscribed or spreading over the surface of the agar and assuming diverse forms, sometimes occupying the whole plate.

Broth.—Turbidity and heavy sediment settling to the bottom of the tube. Slight filmy scum on the surface sticking to the sides of the tube, easily broken up and sinking to the bottom. Slight movements, such as handling the broth tube when transferring it from one place to another, are sufficient to dislodge the film. At no time is a scum like that of *Ps. æruginosa (Bacillus pyocyaneus)* with its firm glistening surface or that of *Bacillus subtilis* with its hard leathery look, formed by *Bacillus coli*.

Gelatine Stab.—Abundant growth along line of inoculation and spreading over the surface of the gelatine. *No liquefaction.*

Gelatine Colonies.—Deep colonies regular, round or oval, brownish in color; superficial colonies, opaque, brownish, slightly spreading.

Potato.—Growth varies from faint white glistening barely perceptible film to an abundant yellowish-brown or even reddish-brown mass covering the entire cut surface of the potato.

The variations in the growth depend more on the nature and composition of the potato than upon any variations in the bacillus itself, as a number of potato tubes inoculated with the same culture will show every conceivable gradation in extent and character of growth.

Fermentation Tube: Dextrose Broth.—Abundant growth in bulb with the production of a turbidity and heavy sediment. Rarely, a faint film on the surface. *Reaction* in bulb *acid.* Abundant growth in closed arm with rapid evolution of *gas.* *Reaction* in closed arm *acid.*

The amount of gas from the dextrose broth varies considerably in quantity, this quantity depending somewhat on the temperature at which the growth takes place, and somewhat upon the character of the culture itself. The first evolution of gas is deceptive, as the fermentation tubes when kept for a number of days allow approximately the same quantity of gas to collect.

Saccharose not broken up to either *acid* or *gas.*

Lactose split up with the production of *acid* and *gas.* The quantity of gas from lactose varies considerably, but if the lactose tubes be observed for some time the amount of gas in the different tubes will be found to reach nearly the same level.

Blood Serum.—Abundant white growth over the surface. *No liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Usually produced abundantly. The amount is greater in old cultures and also in cultures isolated from the lower portion of the intestinal tract. At times cultures from the stomach give positive indol reactions. Again, cultures of organisms which are undoubtedly *Bacillus coli* fail to produce indol.

Fecal Odor.—Usually produced. Not to be regarded as necessary for the identification of *Bacillus coli,* as many cultures fail to exhibit it.

Litmus Milk.—Abundant acidity invariably produced within forty-eight hours. Amount of acid constantly increasing, milk usually coagulated on the second day. When the coagulation of milk takes place early, the coagulation is dense and firm, but white or pink in color. The amount of acid constantly increases, and the coagulum assumes a pink color which is increased in the presence of oxygen. Shaking the tube and breaking up the coagulum produces a deep pink. In other cases an acidity is produced early, but the coagulation is delayed for some days, sometimes for a period of three weeks. *Coagulation always eventually* takes place even though delayed for some time.

Frequently the transfer of the milk tubes from a lower to a higher temperature, as from that of the room to that of the thermostat, will induce coagulation in specimens in which the coagulation has failed to appear. Heating in the gas flame also throws down the casein. The time at which coagulation ensues depends somewhat on the quality of the milk used, as freshly inoculated tubes will occasionally reveal an immediate coagulation with the same bacillus which originally failed to coagulate for days. In two instances, cultures were encountered which coagulated milk within eighteen hours, the coagulum remaining white and colorless. In all other respects this organism corresponded to a typical *Bacillus coli*. Booker, 1889, has also referred to this variety.

Under all circumstances the production of acidity and the coagulation of milk must be regarded as essential to the diagnosis of Bacillus coli. No production of alkali at any period. No peptonization of the casein.

Occurrence and Distribution.—Found in 27 different cases, *i. e.*, in over 50 per cent. of the cases examined by Ford, and thus more frequent than *Bacillus communior* of Durham.

Isolated from the rectum alone in five cases, from the cecum alone in four cases, from the duodenum alone in two cases and from the stomach alone in one case.

Isolated from two portions of the intestinal tract in ten cases; from cecum and rectum in six cases, rectum and duodenum once, rectum and stomach once, and stomach and duodenum twice.

It was obtained from three portions of the intestinal tract in four cases; from stomach, duodenum and cecum twice; from stomach, duodenum and rectum once, and from duodenum, cecum and rectum once. In one case found in the stomach, duodenum, cecum and rectum.

It is thus seen to be one of the most common inhabitants of the intestinal tract, appearing in all its regions, but especially favoring a location in the cecum and rectum, although wandering frequently to the duodenum and stomach, where it grows abundantly and where its cultures produce characteristic reactions on culture media.

26. BACILLUS COMMUNIOR, Ford, 1903.

Literature and Synonym: Bacillus coli communior.—Durham, 1900-1901, Journal of Experimental Medicine, Vol. V, p.

353. Ford, W. W., 1900, Classification Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

As already stated, Durham has called attention to the fact that the variety of *Bacillus coli,* which was originally described by Escherich, is not endowed with the property of fermenting saccharose, and that this variety is not as common in the intestinal tract as the organism fermenting the three sugars. Our observations on the intestinal flora substantiate Durham's conclusions in their main details. There are two great groups of *Bacillus coli* to be separated by their capacity of splitting up saccharose, as has already been mentioned, to one of which the name, *Bacillus coli, Escherich,* is exactly applicable, while for the other the name *Bacillus communior* may be utilized, reserving as a synonym the term originally proposed by Durham, *Bacillus coli communior.*

In regard to the frequency with which these two microorganisms are present in the intestinal contents, Ford was unable to confirm Durham's work. The *Bacillus coli* fermenting saccharose is somewhat less common than the true *Bacillus coli* of Escherich, and thus the name of *Bacillus communior* may not be interpreted numerically, although it be retained as a specific name.

The cultures of *Bacillus communior* agree in all important respects with the pure type of this species, in morphology, motility, none-liquefaction, acid-production and in their reactions with dextrose broth in the fermentation tube. *Saccharose* is fermented, however, with the production of *acidity* and much *gas.*

Occurrence and Distribution.—Obtained by Ford in 26 of 50 examined, as compared with 27 for the type; and in 44 portions of the intestinal tract, as compared with 47 for the type.

Found in one portion of intestinal tract alone in 14 cases, in eight of which it was isolated from the rectum, in two from the cecum, in one from the duodenum, and in three from the stomach. In seven cases it appeared in two regions in the combinations, rectum and cecum three times, rectum and duodenum once, cecum and duodenum once, and duodenum and cecum twice.

In four cases it was obtained from three portions; rectum, cecum and stomach twice, cecum, stomach and duodenum twice. In one case it was obtained from all the different regions of the intestine examined, appearing concurrently

in the stomach, duodenum, cecum and rectum. It thus is present in all portions of the bowel, especially towards the lower end, but is able to occupy the duodenum and stomach as well.

27. BACTERIUM AEROGENES, Migula, 1900.

Literature and Synonyms: Bacterium lactis ærogenes.—Escherich, 1886, Die Darmbacterien des Säuglings, Stuttgart, p. 57.

Bacterium aceticum.—Baginsky, 1888, Zeitschrift f. phys. Chemie, 12, p. 434.

Bacillus ærogenes.—Kruse, 1896, Flügge, Die Mikroorganismen, p. 340.

Bacterium ærogenes.—(Escherich.) Migula. Migula, 1900, System der Bakterien, p. 396.

Bacterium ærogenes.—Escherich. Chester, 1901, Manual of Determinative Bacteriology, p. 128.

First isolated by Escherich from the intestinal contents of infants.

Morphology.—Short stubby bacteria usually measuring 0.75 by 1.0 microns. When stained these forms resemble large cocci. When unstained are seen to be short bacteria. Longer bacteria of the same diameter as the typical forms are frequently met with, their length approximating 2.0 microns, the diameter, however, being identical with that of the short stubby forms. Milk cultures show the development of a capsule, the presence of which contributes to the peculiar thick form of the micro-organism.

The morphology of *Bacterium ærogenes* is always characteristic, and is of prime importance in its identification.

Motility.—Motility cannot be demonstrated at any time either in agar and broth cultures, or in old cultures.

Spores.—Not formed.

Agar Slant.—Abundant thick white glistening growth, usually heaped up at the edges and along the line of inoculation. It often spreads over the surface and slopes to the bottom of the tube. It rarely penetrates deeply beneath the surface of the agar, and it recovers its typical appearance after several inoculations.

Agar Colonies.—Deep colonies, round and regular; superficial colonies, thick, opaque, raised slightly from the surface and circumscribed in outline.

Broth.—Great turbidity, abundant sediment and usual production of scum.

Gelatine.—Thick growth along line of inoculation and spreading over the surface of the gelatine. *No liquefaction.*

Gelatine Colonies.—Deep colonies, round, regular, grayish brown; superficial colonies, thick, opaque, porcelain white.

Potato.—Thick, yellowish-white or yellowish-brown growth with peculiar wart-like elevations along the edges and upon the surface.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Reaction acid in bulb.* Abundant growth in closed arm with the production of an *acid reaction* and much *gas.*

Saccharose and *Lactose* also fermented with the production of *gas* and *acid.*

Blood Serum.—Abundant glistening white growth. *No liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Usually not produced. Occasionally typical cultures of *Bacterium œrogenes* give characteristic and positive reactions for indol.

Litmus Milk.—Acidity produced within eighteen hours. Coagulation of the milk usually within the first twenty-four hours, the coagulum being a pale pink in color. The color deepens with the production of acidity and by the free access of oxygen to the coagulum. The coagulation may be delayed fifteen or twenty days, but always eventually develops. It may frequently be hastened by rapid changes of temperature. Bacteria which, with some specimens of milk coagulate only at a late date, will coagulate other samples within forty-eight hours. Occasionally a perfectly white coagulum is produced in the first day, only a faint acidity developing, analogous to certain cultures of *Bacillus coli. No peptonization of casein.*

Production of acidity and coagulation of milk essential in the identification of *Bacterium œrogenes.*

Occurrence and Distribution.—Isolated by Ford from 31 cases, thus being the most frequent micro-organism in the intestinal tract. In the 31 cases it was found in 56 different regions.

In 12 cases it was obtained from one region of the bowel alone, from the stomach in five cases, from the duodenum in three cases, from the cecum in three and from the rectum in one case. It was found in combination in two regions in

15 cases; in stomach and duodenum four times, in stomach and cecum four times, in stomach and rectum twice, in duodenum and cecum four times, and in the cecum and rectum once.

Three times it was seen in three different portions of the intestinal tract, stomach, duodenum and cecum, once; stomach, cecum and rectum, once; and in the duodenum, cecum and rectum, once. It was obtained from all four regions of the intestines examined in one case, stomach, duodenum, cecum and rectum.

The *Bacterium ærogenes* thus enjoys a very wide distribution in the intestinal contents, being most frequently seen in the stomach and duodenum, but also being carried down to the cecum and rectum, where it dwells side by side with *Bacillus coli.*

28. BACTERIUM DUODENALE, Ford, 1903.

Besides the typical *Bacterium ærogenes,* capable of fermenting three sugars, a micro-organism corresponding in its main cultural features to *Bacterium ærogenes,* but differing in regard to its inability to ferment saccharose, is a common inhabitant of the intestines. To this organism the name *Bacterium duodenale* may be given, indicating its more frequent habitat, the duodenum.

In morphology, lack of motility, non-liquefaction and reactions with the fermentation tube, it agrees with *Bacterium ærogenes.*

It was isolated by Ford from 28 cases and from 45 different regions. It was found in one region alone in 18 cases, in the stomach in five, in the duodenum in three, in the cecum in six and in the rectum in four cases; in stomach and duodenum once; in stomach and rectum once and in the cecum and rectum twice. In five cases it was seen in three regions, stomach, duodenum and cecum three times, and stomach, duodenum and rectum twice. In one case it was found in stomach, duodenum, cecum and rectum.

The *Bacterium duodenale* is thus most frequently found in the stomach and duodenum, but may be carried down to the cecum and rectum. Like *Bacterium ærogenes* it prefers, however, a location in the upper portion of the intestines.

29. BACILLUS GASTRICUS, Ford 1902.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First obtained from the intestinal contents by Ford.

Morphology.—Small bacilli measuring 0.5 by 2-3.0 microns, appearing as single elements or rarely in short chains.

Motility.—Active motility; bacilli move rapidly from one portion of the field to another.

Spores.—Not formed.

Agar Slant.—Glistening white or yellowish white abundant growth, usually limited to line of inoculation.

Agar Colonies.—Deep colonies, round and regular; superficial colonies, thick, opaque, non-spreading.

Broth.—Turbidity, no scum.

Gelatine Stab.—Rapid and complete liquefaction from surface downward, the fluid gelatine forming a thick layer above the solid within twenty-four hours.

Gelatine Colonies.—Deep colonies, round and regular; superficial colonies, of various dimensions, opaque with dark centers and slightly spreading periphery.

Potato.—Luxuriant brownish or brownish-red growth.

Fermentation Tube: Dextrose Broth.—Abundant growth in open bulb with the production of turbidity and a heavy sediment. *Reaction acid* in bulb. Growth in closed arm with the evolution of *gas* and an *acid reaction.*

Saccharose and *Lactose* also fermented with the production of *acidity* and *gas.*

Blood Serum.—Abundant dark-yellow or greenish-brown growth. *No liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Usually produced.

Fecal Odor.—Usually produced.

Litmus Milk.—Rapid production of acidity, coagulation of the milk, coagulum dense and firm. No *peptonization of the casein.*

30. BACILLUS SUBGASTRICUS, Ford, 1902.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

An organism differing from *Bacillus gastricus* in not fermenting saccharose, but in agreeing with it in its general cultural features was isolated from two cases.

To this bacillus the name *Bacillus subgastricus* may be given. It was obtained from the stomach and duodenum in one case, and from the duodenum and cecum in another.

31. BACTERIUM LIQUEFACIENS Eisenberg, 1892, Ford, 1902.

Literature and Synonym: Bacillus liquefaciens.—Eisenberg, 1892. Bakt. Diagnostik, p. 13.

Originally obtained by Eisenberg from feces, later from water.

Morphology.—Broad, thick bacteria, measuring 0.75 by 2.0 in dimensions.

Motility.—Non-motile.

Spores.—Not formed.

Agar Slant.—White glistening abundant growth, thick and heaped up along line of inoculation, but not spreading or sloping.

Agar Colonies.—Deep colonies, round and regular; superficial colonies, large, round, opaque, circumscribed, varying greatly in size.

Broth.—Turbidity, no scum.

Gelatine Stab.—Slow growth along line of inoculation; cone-like liquefaction appearing on the fifth or sixth day and progressing slowly; no surface growth.

Gelatine Colonies.—Deep colonies, round and regular; superficial colonies, slightly spreading, grayish, looking like broken glass when thickly sewn.

Potato.—Luxuriant dirty-brown growth.

Fermentation Tube: Dextrose Broth.—Abundant growth in bulb with turbidity and sediment. *Reaction* in bulb *acid.* Growth in closed arm with the evolution of *gas* and the production of an *acid reaction.*

Saccharose and *Lactose* also fermented to *acid* and *gas.*

Blood Serum.—Abundant yellowish growth. *No liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Abundant.

Fecal Odor.—Frequently present.

Litmus Milk.—Acidification and coagulation of the milk within forty-eight hours. *No peptonization* of the casein.

32. BACTERIUM SUBLIQUEFACIENS, Ford, 1902.

Organisms agreeing in their main cultural features with the preceding, but failing to ferment saccharose, are more

frequently present in the intestines than are the typical form. To them the name *Bacterium subliquefaciens* may be given. They were met with in three cases, once in the duodenum, once in the cecum, and once in combination in the stomach and rectum.

33. BACILLUS CLOACÆ, Jordan, 1890.

Literature.—Jordan, 1890, Report of the State Board of Health of Massachusetts, Part XI, p. 836.
Migula, 1900, System der Bakterien, p. 722.
Chester, 1901, Manual of Determinative Bacteriology, p. 232.
First obtained by Jordan from sewage.

Morphology.—Short thin bacilli, measuring 0.5-1.0 by 1-2.0 microns.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Porcelain-white glistening growth, spreading over the surface of the agar.

Agar Colonies.—Deep colonies, round and regular; surface colonies thick, opaque, round, or with opaque white centers with thin outlying periphery.

Broth.—Turbidity and frequently a thin scum.

Gelatine Stab.—Complete, usually rapid liquefaction, fluid gelatine lying above the solid medium. In certain cultures the liquefaction is very slow.

Gelatine Colonies.—Deep colonies, round, regular, yellowish; superficial colonies, thin, bluish, translucent.

Potato.—Luxuriant dull-white or yellowish-white growth.

Fermentation Tube: Dextrose Broth.—Sediment and turbidity in bulb; *reaction acid.* Abundant growth in closed arm. Evolution of *gas* and an *acid reaction.*
Saccharose and *Lactose* alike fermented to *acid* and *gas.*

Blood Serum.—Abundant growth, *liquefaction slow, but complete* after ten to twelve days.

Nitrates.—Reduced to nitrites.

Indol.—Usually produced.

Fecal Odor.—Usually present.

Litmus Milk.—Slow development of acidity and eventual coagulation of the milk. Gradual *peptonization* of the casein.

34. BACILLUS SUBCLOACÆ, Ford, 1902.

Organisms corresponding to *Bacillus cloacæ* in all respects except in their fermentation of saccharose may conveniently be grouped together under the name *Bacillus subcloacæ*. They were isolated from the intestinal contents in five cases, from stomach, duodenum, cecum and rectum separately once, and from the duodenum, cecum and rectum together once.

35. BACILLUS ILIACUS, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

Morphology.—Very large bacilli measuring 0.75 by 3-4.0 microns, appearing invariably as single elements.

Motility.—Actively motile, the bacilli shooting rapidly from one portion of the field to another.

Spores.—Not formed.

Agar Slant.—White glistening growth spreading over the whole surface of the agar.

Agar Colonies.—Deep colonies, round and regular; superficial colonies, opaque, spreading rapidly over the surface, with thick opaque centers and thin translucent margins.

Broth.—Turbidity and thick scum.

Gelatine Stab.—Rapid growth along line of inoculation with complete liquefaction of the gelatine from the surface downward.

Gelatine Colonies.—Deep colonies, regular, slightly brown; superficial colonies, large, translucent and spreading.

Potato.—Abundant yellowish-brown growth.

Fermentation Tube: Dextrose Broth.—Rapid growth in bulb with the production of a scum and turbidity. *Reaction acid.* Growth in closed arm with the evolution of *gas* and the formation of *acid.*

Saccharose also fermented with the production of *gas* and *acidity.*

Lactose not broken up to either *acid* or *acid* and *gas.*

Blood Serum.—Abundant dull-brown growth with a rapid and complete liquefaction.

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Rapid acidification and coagulation with an early *peptonization* of the casein and a reduction of the litmus.

36. BACILLUS CHYLOGENES, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First obtained from intestinal contents by Ford.

Morphology.—Small, fine bacilli, measuring about 0.5 by 1.0 microns, appearing as diplo-bacilli which, when stained, look like diplococci.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Pale, almost transparent film, almost invisible even after the lapse of forty-eight hours.

Agar Colonies.—Deep colonies, very fine pale brown; superficial colonies, oblong or nail-shaped, very small, pale brown in color; growth very slow.

Broth.—Marked turbidity after forty-eight to seventy-two hours. No scum.

Gelatine Stab.—Slow growth along line of inoculation, with beginning *liquefaction,* which is completed only after 6 to 8 days.

Gelatine Colonies.—Small, round, regular, non-characteristic, deep and superficial colonies.

Potato.—Growth varies from a scanty white to a pale yellow brown appearing after forty-eight hours.

Fermentation Tube: Dextrose Broth.—Turbidity in bulb with a scanty sediment. *Reaction acid* in *bulb.* Slow growth in closed arm. *Reaction* in *arm acid. No gas.*

Saccharose and *Lactose* not fermented to *acid* alone nor to *acid* and *gas.*

Blood Serum.—Abundant pale white growth developing very slowly, but not producing any liquefaction.

Nitrates.—No reduction to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Within forty-eight hours production of a slight acidity which constantly increases till the milk is coagulated, and a pink color is eventually produced. *No peptonization of casein.*

37. BACTERIUM CHYMOGENES, Ford, 1903.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First obtained by Ford from intestinal contents.

Morphology.—Bacteria measuring 0.5 by 2.0 microns in dimensions.

Motility.—Non-motile.

Spores.—Not formed.

Agar Slant.—Abundant white glistening growth, heaped up above line of inoculation.

Agar Colonies.—Deep colonies, round and regular; surface colonies, large, opaque, round, circumscribed, varying greatly in size.

Broth.—Turbidity, no scum.

Gelatine Stab.—Slow growth along line of inoculation; slow *liquefaction* complete after seven to eight days.

Gelatine Colonies.—Deep colonies, round, regular; superficial colonies, large, regular, refractile, non-characteristic.

Potato.—Luxuriant dirty brown growth.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Reaction* in bulb *acid.* Growth in closed arm with the production of *acidity,* but no *gas.*

Saccharose and *Lactose* not fermented, to either *acid* or *acid* and *gas.*

Blood Serum.—Abundant growth, yellowish-white. *No liquefaction.*

Nitrates.—Not reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Acidification and coagulation within forty-eight hours. *No digestion* of the casein.

38. BACILLUS LEPORIS, Migula, 1900.

Literature and Synonyms: Bacillus leporis lethalis.—Sternberg, 1890, Text-book of Bacteriology, p. 478.

Bacillus leporis (Sternberg) Migula.—Migula, 1900, System der Bakterien, p. 651.

Bacillus leporis (Sternberg).—Chester, 1901, Manual of Determinative Bacteriology, p. 243.

Isolated first by Gibier and later by Sternberg from the contents of the intestine in yellow fever.

Morphology.—Very long, thin bacilli measuring 0.5 by 4-6.0 microns, always made up of long single elements and never appearing in chains.

Motility.—Bacilli are very actively motile, shooting rapidly from one portion of the field to another with the velocity of a culture of *Proteus æruginosa (Bacillus pyocyaneus).*

Spores.—Not formed.

Agar Slant.—Abundant white glistening growth in young cultures, but rapidly drying and turning brown in old cultures.

Agar Colonies.—Deep colonies, round and uniform; surface colonies, round, slightly spreading, with serrated edges, grayish in color.

Broth.—Turbidity, no scum.

Gelatine Stab.—Abundant growth, rapid and complete liquefaction, beginning at the surface and proceeding downwards.

Gelatine Colonies.—Deep colonies, round, translucent, light-yellow; surface colonies, transparent, spreading, with broken glass appearance.

Potato.—Luxuriant yellowish-brown growth within three to four days.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Acid reaction.* Growth in closed arm with the production of an *acid reaction* but no *gas.*

Saccharose and *Lactose* alike fermented to *acid* but no *gas.*

Blood Serum.—Abundant growth in twenty-four hours. Rapid and complete *liquefaction* of the blood serum.

Nitrates.—Reduced to nitrites.

Indol.—Usually produced.

Fecal Odor.—Rarely produced.

Litmus Milk.—Rapid acidification and coagulation of the milk No *peptonization* of the casein or reduction of the litmus.

39. BACILLUS DUBIUS, Kruse, 1896.

Literature.—Bleisch, 1893, Zeitschrift für Hygiene, Vol. XIII, p. 31. Flügge, 1896, Die Mikroorganismen. Chester, 1901, Manual of Determinative Bacteriology, p. 237.

First isolated from feces by Bleisch.

Morphology.—Short, thin bacilli measuring 0.75 by 2.0 microns, sometimes appearing in pairs.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Abundant glistening, yellowish growth, turning brown in old cultures.

Agar Colonies.—Deep colonies, round, regular, opaque; superficial colonies, grayish, spreading over surface, corrugated or skein-like in appearance.

Broth.—Turbid, no scum.

Gelatine Stab.—Abundant growth along line of inoculation. Rapid and complete liquefaction, usually within three days.

Gelatine Colonies.—Deep colonies, round and regular; superficial colonies, fine, irregular, slightly spreading, grayish brown.

Potato.—Abundant yellowish-brown glistening mass.

Fermentation Tube: Dextrose Broth.—Abundant growth in bulb with a heavy sediment. *Reaction in bulb acid.* Abundant growth in closed arm with an *acid reaction* but no *gas.*

Saccharose and *Lactose* not fermented to acid or gas.

Blood Serum.—Yellowish growth and a slow but complete liquefaction.

Nitrates.—Reduced to nitrites.

Indol.—Produced in small quantities.

Fecal Odor.—Produced in small amount.

Litmus Milk.—Acidification and coagulation within forty-eight hours. Slow and complete peptonization of the casein with a reduction of the litmus.

40. BACILLUS JEJUNALIS, Ford, 1902.

Literature.—Ford, W. W., 1901, Classification of Intestinal Bacteria, Journal of Medical Research, Vol. I, p. 211.

First isolated from intestinal contents by Ford.

Morphology.—Short bacilli measuring 0.5 by 2.0 microns, appearing as single elements or as long chains.

Motility.—Actively motile.

Spores.—Not formed.

Agar Slant.—Abundant thick white growth within forty-eight hours.

Agar Colonies.—Deep colonies, round, regular, dark brown; superficial colonies, may be large, translucent, pale blue, or spreading, with opaque centers and filmy transparent margins, assuming star shapes or bizarre shapes.

Broth.—Turbidity but no scum.

Gelatine Stab.—Abundant growth. Rapid and complete liquefaction.

Gelatine Colonies.—Deep colonies, fine, brown, regular; superficial colonies are large, irregular, slightly spreading, dark brown in color.

Potato.—Luxuriant glistening white growth.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Reaction* in bulb *acid.* Abundant growth in closed arm with the production of *acidity* but no *gas.*

Saccharose and *Lactose* not fermented to acid or gas.

Blood Serum.—Slow white growth, becoming very luxuriant after eight to ten days, and causing a complete liquefaction of the medium.

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Acidification and coagulation within forty-eight hours. Slow peptonization of the casein but no reduction of the litmus.

41. PSEUDOMONAS ÆRUGINOSA (Schröter, 1872), Migula, 1900.

Literature and Synonyms.—Bacterium æruginosum. Schröter, 1872, Ueber einige durch Bakterien gebildete Pigmente, Cohn's Beiträge zur Biologie, Bd. I, p. 126.

Bacillus æruginosus. Schröter, 1872. Schröter, 1886, Kryptog. Enc. Flora von Schlesien, Bd. III, p. 157.

Bacillus pyocyaneus. Gessard, 1882, De la pyocyanine et de son microbe, Thèse de Paris.

Pseudomonas pyocyanea. Migula, 1896, Die Natürlichen Pflanzenfamilien.

Pseudomonas pyocyanea (Gessard) Migula. Chester, 1901, Manual of Determinative Bacteriology, p. 321. Migula, 1896, System der Bakterien, p. 884.

First accurately described by Gessard in 1882. Found frequently on the surface of the body, in the mouth, intestines, and in many pathological conditions.

Morphology.—Fine bacilli measuring 0.5 by 2.0 microns, appearing as single elements, pairs and short chains.

Motility.—Actively motile, bacilli shooting rapidly from one portion of the field to another.

Spores.—Not formed.

Agar Slant.—Abundant glistening white growth within twenty-four hours, rapidly producing a bright green pigment which

is imparted to the medium. The growth itself rapidly turns dark brown.

Agar Colonies.—Deep colonies, round and regular, yellowish; superficial colonies, large, spreading with darker centers and translucent edges, assuming various bizarre formations and producing a green color in the surrounding agar.

Broth.—Great turbidity and heavy tenacious scum rapidly formed. Bright green fluorescence produced.

Gelatine Stab.—Abundant growth along line of inoculation and on the surface. Rapid liquefaction of the gelatine which assumes a bright green color.

Gelatine Colonies.—Deep colonies, round and regular, yellowish; superficial colonies, yellowish or greenish yellow, fringed, irregular, producing a skein-like formation.

Potato.—Luxuriant dirty-brown growth, the potato assuming a greenish color.

Fermentation Tube: Dextrose Broth.—Abundant turbidity with the formation of thick scum. *Reaction* of bulb *alkaline. No growth* in *closed arm.* Dextrose broth assumes a bright green color.

Saccharose and *Lactose* also show a heavy scum and assume a bright green color.

Blood Serum.—Rapid growth, the serum turning bright green and rapidly being liquefied.

Nitrates.—Not reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced, in its place a characteristic odor of trimethylamin.

Litmus Milk.—Reaction of litmus unchanged; no acid production, no coagulation. Rapid digestion of the casein and reduction of the litmus.

Fluorescence and *Chromogenesis.*—Greenish.

Occurrence and Distribution.—Frequently present in the intestinal contents. Found in nine cases, being isolated from one portion of the intestines alone in five cases, four times from the rectum and once from the cecum. In one case found in the duodenum and rectum. In three cases it was isolated from every portion of the intestines, appearing simultaneously in stomach, duodenum, cecum and rectum.

42. PSEUDOMONAS OVALIS (Ravenel, 1896), Chester, 1901.

Literature and Synonym.—Bacillus fluorescens—ovalis. Ravenel, 1896, Memoirs National Academy of Sciences, No. 9.

Pseudomonas ovalis. Chester, 1901, Manual of Determinative Bacteriology, p. 325.

First obtained from the soil by Ravenel.

Morphology.—Very fine bacilli measuring 0.5 by 2.0 microns, appearing usually as single elements.

Motility.—Actively motile. Bacilli shoot rapidly from one portion of the field to another.

Spores.—Not formed.

Agar Slant.—Thick, white abundant growth. No pigment production. Green fluorescence produced only in six to eight days.

Agar Colonies.—Deep colonies, fine, colorless; superficial colonies, round, regular, circumscribed, opaque, gradually producing a greenish fluorescence.

Broth.—Scum and turbidity.

Potato.—Luxuriant dirty brown growth.

Fermentation Tube: Dextrose Broth.—Turbidity in bulb. Scum on surface of broth. *Reaction* in bulb *alkaline.* No growth in closed arm. Abundant green fluorescence.

Saccharose and *Lactose* show a green fluorescence, scum on surface, but no fermentation.

Gelatine Stab.—Abundant growth along line of puncture. *No liquefaction.*

Gelatine Colonies.—Deep colonies, fine, regular, colorless; superficial colonies, irregular, with faint prolongations, which give a granular appearance like broken glass.

Blood Serum.—Abundant growth without liquefaction.

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—No preliminary acidity. Alkali production immediate. No coagulation of the milk. No digestion of the casein. No reduction of the litmus.

Fluorescence.—Green in all fluid cultures and in old agar tubes. No chromogenesis.

43. BACTERIUM HAVANIENSE (Sternberg, 1892), Chester, 1901.

Literature and Synonym: Bacillus Havaniensis.—Sternberg, 1892, Manual of Bacteriology, p. 718. (Not *Bacillus Havaniensis* of Migula, 1900.)

Bacterium Havaniense (Sternberg.) Chester, 1901, Manual of Determinative Bacteriology, p. 178.

First isolated by Sternberg from the intestinal contents of yellow fever cadavers.

Morphology.—Short, fine bacteria measuring 0.5 by 0.75 microns, in stained preparations looking like micrococci or diplococci. In unstained preparations seen to be true bacteria.

Motility.—Non-motile.

Spores.—Not formed.

Agar Slant.—Bacteria grow rapidly on agar, forming a dull, thick, white growth. Occasionally a carmine red growth is produced at the temperature of the body within twenty-four hours, but usually the pigment production is delayed for forty-eight to seventy-two hours. Pigment is formed at the edge of the growth, which after six to eight days is completely colored. Cultures freshly isolated from the intestine show a much more rapid pigment production. Growth never tenacious. *No fluorescence.*

Agar Colonies.—Deep colonies, round and regular, colorless; superficial colonies may be white, opaque or carmine red, with other colonies showing gradations between the two. The colonies are usually white with reddish margins. In the same plate all the varieties of colonies may be seen. After the lapse of forty-eight or seventy-two hours the colonies all become carmine red.

Broth.—Turbidity and heavy scum. No fluorescence.

Gelatine Stab.—Rapid growth and complete liquefaction. Gelatine turned a brilliant red.

Gelatine Colonies: Characteristice appearance.—Gelatine is liquefied within twenty-four hours, and assumes a bright red color. Floating about in the liquefied gelatine are numerous small colonies with dark red centers and lighter peripheries. No odor from gelatine plate.

Potato.—Luxuriant growth, at first white but rapidly becoming a dark red.

Fermentation Tube: Dextrose Broth.—Heavy scum and great turbidity. *Reaction acid.* Growth in closed arm. *Acid reaction. No gas.*

Saccharose fermented to *acid* and *gas.*
Lactose not fermented to *acid* or *gas.*

Blood Serum.—Abundant carmine red growth. *No liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Reaction of milk remains unchanged. No demonstrable production of acid or alkali. Coagulation of the milk with digestion of the casein and reduction of the litmus.

44. BACTERIUM LUTESCENS, Migula, 1900.

Literature and Synonym: Der gelbe Bacillus.—Migula, 1900, System der Bakterien, p. 476. Lustig, 1893, Diagnostik der Bakterien des Wassers, p. 78.

First isolated by Lustig from water.

Morphology.—Short bacteria measuring 0.5 by 0.75 microns, appearing like cocci and diplococci in stained preparations.

Motility.—Non-motile.

Agar Slant.—Growth slow. Pale yellow at first, later turning to a golden yellow. *No fluorescence.*

Agar Colonies.—Deep colonies, round, regular and pale yellow; superficial colonies, circumscribed, white colonies later becoming golden yellow.

Broth.—Turbidity, no scum. No fluorescence.

Gelatine Stab.—Slow growth. Gradual complete liquefaction.

Gelatine Colonies.—Deep colonies, round, circumscribed; superficial colonies, fine, round, with slight peripheral extensions, gradually becoming golden yellow.

Potato.—Luxuriant golden yellow growth.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Reaction alkaline.* No growth in closed arm.

Saccharose and *Lactose* also not fermented.

Blood Serum.—Abundant yellowish growth; *no liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—No preliminary acidity. Alkali production immediate. No coagulation of the milk. No digestion of the casein.

Chromogenesis, yellow. *No fluorescence.*

First isolated from the air by the Franklands.

Morphology.—Long, thick bacilli, measuring 0.75 by 2-4.0 microns in dimensions, not showing polar staining. Frequently growing in long chains.

Motility.—Actively motile.

Spores.—Formed rapidly on all media.

Agar Slant.—Abundant growth, at first white and glistening, later becoming a dirty brown. Not dull or wrinkled.

Agar Colonies.—Deep colonies, round, regular and grayish; superficial colonies spread over the surface of the agar, showing dark centers and outlying gray peripheries, and assuming diverse bizarre shapes.

Broth.—Turbidity and scum.

Gelatine Stab.—Abundant growth. Rapid and complete liquefaction.

Gelatine Colonies.—Deep colonies, small, round and regular; superficial colonies have dark centers and spreading peripheries made up of long, thin threads.

Potato.—Faint, scanty white growth.

Fermentation Tube: Dextrose Broth.—Turbidity and heavy scum in bulb. *Reaction alkaline.* No growth in closed arm.

Saccharose and *Lactose* not fermented. Abundant scum on all sugar media.

Blood Serum.—Abundant white, moist growth without liquefaction.

Nitrates.—Not reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—No preliminary acidity. Alkaline reaction. No coagulation.

Digestion of the casein and reduction of the litmus.

48. BACILLUS MYCOIDES, Flügge, 1886.

Literature.—Flügge, 1886, Die Mikroorganismen, 2 Aufl. Migula, 1900, System der Bakterien, p. 538.

Isolated from water and soil by Flügge.

Morphology.—Bacilli measuring 1-1¼ by 3-4 microns in dimensions, occurring in pairs and chains.

Motility.—Actively motile.

Spores.—Formed rapidly on all media.

Agar Slant.—Growth along line of inoculation dull, wrinkled and tenacious, with difficulty raised from the surface of the agar, into which it sinks for a considerable depth.

Agar Colonies.—Deep colonies, round, regular and opaque; superficial colonies spread over the surface of the agar assuming diverse sizes and shapes, but gradually fusing and forming a thick network.

Broth.—Turbidity and wrinkled scum.

Gelatine Stab.—Rapid and complete liquefaction, with a heavy scum on the surface.

Gelatine Colonies.—Deep colonies, round, regular and opaque; superficial colonies, bluish-gray, with light opaque centers and dark spreading peripheries. As colonies become older they coalesce, forming a skein-like mycelium.

Potato.—Thick white abundant growth.

Fermentation Tube: Dextrose Broth.—Turbidity in bulb, with a heavy scum on the surface. *Reaction acid.* Growth in closed arm with the production of acid but no gas.

Saccharose and *Lactose* not fermented.

Blood Serum.—Abundant white growth. *No liquefaction.*

Nitrates.—Reduced to nitrites. Heavy scum on nitrate broth.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Preliminary acidity followed by an alkaline reaction. No coagulation. Digestion of the casein and reduction of the litmus.

49. BACTERIUM LACTICOLA, Migula, 1900.

Literature and Synonym.—Flügge, 1894, Die Aufgaben und Leistungen der Milchsterilisierung gegenüber die Darmbakterien des Säuglings, Zeitschr. f. Hygiene, Bd. XVII, p. 294.

Bacillus lactis, No. V.—Kruse, 1896. Flügge, Die Mikroorganismen, 3 Aufl, Bd. II, p. 28. Migula, 1900, System der Bakterien, p. 305.

First obtained by Flügge from milk.

Morphology.—Long, thin bacteria measuring 1.0 by 3-5.0 microns, occurring in short chains and showing polar staining.

Motility.—Non-motile.

Spores.—Formed quickly on all media.

Agar Slant.—Dull wrinkled growth in young cultures, rapidly spreading over whole surface of the agar.

growth made up of long processes, which cover the entire surface of the potato with a corrugated mass.

Fermentation Tube: Dextrose Broth.—Turbidity and membrane in bulb. *Alkaline reaction* in *bulb.* No growth in closed arm.

Saccharose and *Lactose* not fermented.

Blood Serum.—Abundant growth. Complete liquefaction.

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—No preliminary acidity. Rapid production of alkali. No coagulation. Peptonization of the casein and reduction of the litmus.

52. BACILLUS BREVIS, Migula, 1900.

Literature and Synonym: (Bacillus No. 1).—Flügge, 1894, Die Aufgaben und Leistungen der Milchsterilisierung, Zeitschrift für Hygiene, Bd. XVII, p. 294. Migula, 1900, System der Bakterien, p. 583.

First obtained by Flügge from milk.

Morphology.—Long, thin bacilli measuring 0.5 by 3.0 microns, often appearing in long chains.

Motility.—Actively motile.

Spores.—Rapidly formed on the usual media.

Agar Slant.—Abundant soft glistening brown growth covering whole surface and not becoming dull or wrinkled.

Agar Colonies.—Deep colonies, round and regular; superficial colonies, round, opaque, non-spreading.

Broth.—Turbidity without scum.

Gelatine Stab.—Slow but complete liquefaction.

Gelatine Colonies.—Round, irregular, brown colonies, often forming a network of fine threads.

Potato.—Little or no growth.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Reaction alkaline.* No growth in closed arm.

Saccharose and *Lactose* not fermented.

Blood Serum.—Abundant growth with complete liquefaction.

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Slight acidity without coagulation, followed by digestion of the casein and reduction of the litmus.

53. BACILLUS SUBTILIS (Ehrenberg 1838), Cohn, 1872.

Literature and Synonym: Vibrio subtilis.—Ehrenberg, 1838, Infusionsthierschen als volkommene Organismen, Leipzig.

Bacillus subtilis.—Cohn, 1872, Beiträge zur Biologie, Bd. I, p. 175.

Bacillus subtilis (Ehrenberg), Cohn.—Migula, 1900, System der Bakterien, p. 515.

Bacillus subtilis (Ehrenberg), Cohn.—Chester, 1901, Manual of Determinative Bacteriology, p. 276.

First obtained by Ehrenberg from air and water.

Morphology.—Bacilli measuring 0.5 by 4-6.0 microns, without polar staining, appearing rarely in short chains.

Motility.—Actively motile.

Spores.—Formed rapidly, lying in the centers of the bacilli.

Agar Slant.—Glistening, dull white, sticky, matted tenacious growth.

Agar Colonies.—Deep colonies, round and regular; superficial colonies spread slightly, with opaque white centers assuming various bizarre shapes.

Broth.—Turbidity and heavy scum.

Gelatine Stab.—Abundant growth, with a rapid liquefaction and a heavy scum on the surface.

Gelatine Colonies: Characteristic appearance.—Deep colonies, round, regular and opaque; superficial colonies spreading with dense black centers and grayish-outlying threads.

Potato.—Luxuriant, thick, grayish or yellowish-brown growth, which in old cultures forms a corrugated stringy mass covering the whole surface of the potato.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Reaction* in bulb *acid.* Growth in closed arm with the production of an acid reaction but no gas.

Saccharose and *Lactose* not fermented.

Blood Serum.—Abundant white growth. *Rapid liquefaction.*

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Rapid acidification and coagulation of the milk; peptonization of the casein and reduction of the litmus.

54. BACILLUS ARACHNOIDEUS, Migula, 1900.

Literature and Synonym: (*Bacillus* No. 111).—Flügge, 1894, Die Aufgaben und Leistungen der Milchsterilisierung, Zeitschrift für Hygiene, Bd. XVII, p. 294. Migula, 1900, System der Bakterien, p. 583.

First isolated by Flügge from milk.

Morphology.—Fine bacilli measuring 0.5 by 2.0 microns. No polar staining, often grows in short chains.

Motility.—Actively motile.

Spores.—Formed rapidly on the usual media.

Agar Slant.—Dull, wrinkled, tenacious growth, sinking deeply beneath the surface of the agar.

Agar Colonies.—Deep colonies, round and regular; superficial colonies, grayish, spreading, with white opaque centers.

Broth.—Turbidity without scum.

Gelatine Stab.—Rapid liquefaction.

Gelatine Colonies.—Deep colonies, regular, uniform; superficial colonies, slightly spreading, grayish with opaque centers, somewhat resembling colonies of *Bacillus subtilis.*

Potato.—Luxuriant yellowish-brown growth, forming huge blebs.

Fermentation Tube: Dextrose Broth.—Turbidity and sediment in bulb. *Reaction* in bulb *acid.* Abundant growth in closed arm with the production of an *acid reaction* but *no gas.*

Saccharose fermented with the production of ***acidity*** and a small quantity of *gas.*

Lactose not fermented.

Blood Serum.—Abundant white growth. ***Rapid liquefaction.***

Nitrates.—Reduced to nitrites.

Indol.—Not produced.

Fecal Odor.—Not produced.

Litmus Milk.—Acidity and coagulation of the milk within forty-eight hours. Peptonization of the casein and reduction of the litmus.

Other bacteria which have been found in the feces, but the full descriptions of which cannot be here included, are:

55. *Bacillus aquatilis sulcatus.*

Short motile bacilli, no spores, obligate anærobes. Gram. —; small, superficial, opalescent colonies, not liquefying gelatine. A yellow pellicle on potatoes. No indol. No fermentation of sugar.

No coagulation of milk. Described by Weichselbaum; five types belonging to the typhoid group.

56. *Bacillus coli immobilis.*

Biological characters those of Bacillus coli, but immobile.

57. *Bacillus coprogenes parvus.*

Short, immobile forms, staining most intensely at the extremities. No spores. Anærobic. Gram. —. Gelatine plates: small, round, light brown, non-liquefying colonies. Gelatine stab: nail-shaped growth. Agar: thin, white colonies. Potato: gray pellicle. Bouillon is clouded. Milk, coagulated with acid formation. Indol formed. Pathogenic for mice and rabbits.

57. *Bacillus fœtidus.*

Various lengths. Motile. Large spores. Gelatine: large colonies liquefied.

58. *Bacillus œdematis ærobius.*

Various sized bacilli. Motile. Facultative anærobes. Gelatine plates: superficial, transparent, opalescent colonies, with wavy margins; deep colonies, round and yellow. In gelatine stabs develop stinking gas. Potatoes: dirty gray pellicle. Bouillon turbid. Pathogenic for guinea pigs, etc., with production of a bloody, œdematous infiltration.

58. *Bacillus putrificus.*

Long (5-6 micra), narrow bacilli. Actively motile. End spores anærobic. Gelatine stab: single colonies, with gas bubbles, which later coalesce; liquefaction. Plates: yellow, opalescent colonies. Gram. +. Spore formation. The bacillus of proteid decomposition.

59. *Bacillus tuberculosis* (Koch).

Slender, slightly curved formed; non-motile. Generally single or parallel; short threads also. No spores. Acid-fast. Stained according to Ziehl-Neelson. Gram. +. Ærobic. For further characters, see text-books.

59. *Bacillus phlei.*

Short, thick bacilli, often enlarged at one extremity. Non-motile. Stain as tubercle bacilli (acid-fast), but also easily with

methylene blue. Growth is far more active than in case of tubercle bacillus, and proceeds at temperatures of 20-25 degrees. Gelatine plates: small, white, irregular colonies. Agar plates: slight growth. Glycerine agar, dense, orange-yellow, plicated growth. Bouillon pellicle, no turbidity.

60. *Bacillus Breslavianus.*

Short, motile bacilli. No spores. Gram. —. Growth resembles coli, except that milk is not coagulated, and no indol is formed. Gas fermentation.

STREPTOCOCCI.

61. *Streptococcus coli gracilis.*

Found in feces and meconium. Temperature 0. 39°. Gelatine plates: small, round colonies, which rapidly liquefy the medium. Gelatine stab: stocking-like liquefaction. Agar: slight growth. Potatoes: small, white, slightly-raised colonies. Non-pathogenic.

62. *Streptococcus coli brevis.*

Found in milk, and in the feces of milk-fed infants. Small cocci, grouped in short chains, the chains often containing single larger forms (so-called megacocci). Gelatine plates: rounded colonies, with shallow, saucer-like liquefaction; center olive-green. Agar: greenish-yellow growth. Blood serum: citron-yellow colonies, no liquefaction.

63. *Streptococcus pyogenes.*

The typical cocci of suppurative processes. May be arranged in long chains *(S. longus)*, or in network *(S. conglomeratus)*, or in short chains *(S. brevis)*. Gram. +. Facultative anærobe. Gelatine plates: small, transparent colonies, with fine granulation, slightly-raised border, no liquefaction. Gelatine stab: granular growth. Agar plates: as in gelatine, but larger. Agar stab: small, isolated colonies along stab, often a delicate surface growth. Potato: no growth. Bouillon: generally clear; sediment. Milk, coagulated.

STAPHYLOCOCCI.

Staphylococci are grouped, according to the coloring matter produced by their colonies, as:

64. *Staphylococcus albus.*

No coloring matter.

65. *Staphylococcus aureus.*

Golden-yellow coloring matter.

66. *Staphylococcus citreus.*

Citron-yellow coloring matter.

The following types of vibriones have been described:

SPIRILLA.

67. *Spirillum choleræ Asiaticæ.*

Three-quarters to two micra long, thickness one-third of length. S and E forms occur; threads and spirilli occur only under circumstances unfavorable to growth. Monotrichons, motile. No spores. Facultative anærobes. Gram. —. Gelatine plates: in twenty-two to twenty-four hours, barely visible colonies, which, under weak magnification, appear as light yellow, granulated, irregularly-rounded colonies, flattened, with slightly raised border. Rapid growth; delicate marginal processes, center yellowish; liquefaction. Colonies shimmer, but zone of liquefaction is dull, and contains grayish fragments. Gelatine stab: growth along stab, with tube-like liquefaction, funnel-like liquefaction at surface. Agar plates: grayish brown, transparent, rounded colonies. Agar slant: grayish-white growth. Blood serum: liquefied. Bouillon: turbidity and pellicle. Cholera-red reaction: on addition of a few drops of pure, strong H_2SO_4 to a twenty-four hours' bouillon growth. Pathogenic for guinea pigs, etc.

68. *Spirillum Gottschlich* (Cholera Nostras).

Growth on all media very similar to Choleræ Asiaticæ. No nitrosoindol, but only indol reaction. Almost all cultures develop much H_2S.

69. *Spirillum helcogenes.*

Found in diarrhea. Similar to bacillus proteus. No nitrosoindol reaction.

70. *Spirillum Lisbon.*

Found in an epidemic in Lisbon.

71. *Spirillum Massanah.*

Found in a case resembling cholera in Massanah.

72. *Spirillum proteus* (Finkler Prior).

For full details regarding these forms, reference must be had to Migula, or other bacteriological system.

CHAPTER XVII.

ANIMAL PARASITES—PATHOLOGICAL FORMS.

PROTOZOA.

The protozoa have of recent years assumed a rôle of some importance in the etiology of intestinal disease, and of this group of animalcules, by all odds the most important is the *Amœba.*

This rhizopod appears, like so many other pathogenic forms, to be a harmless denizen of the gut under ordinary circumstances. At all events, it is possible to find amœbæ in the stools of perfectly normal individuals. They increase in number as the stools become more alkaline in reaction, as, for example, when Rochelle salts are taken daily.

The amœba occurs in the stools in enormous numbers, chiefly imbedded in the mucus, in certain forms of dysentery. Not only is it found in the stools, but pathological examination of the ulcers in the intestine discloses the fact that the organism has worked its way into the ulcers, and has invaded the deeper layers of the intestine.

Notwithstanding these facts, there has always been a school of pathologists which asserts that the amœba is not the actual cause of the disease, but a mere saprophyte, which thrives under the conditions presented by the intestinal contents in cases of so-called amœbic dysentery. This school is of the opinion, then, that some other organism, possibly streptococcus, which occur in large numbers in many cases of the disease, is the real *causa morbi,* and the amœba simply a harmless symbiote. They would compare its rôle to that of the *Aspergillus,* which is occasionally found luxuriantly growing in the lung cavities which have been produced by the action of the tubercle bacillus. That there is some ground for this theory cannot be disputed. Indeed, the history of coprology presents several instances of similar fallacious conclusions.

On the other hand, there are certain arguments which speak very strongly for the pathogenic and etiological rôle of the amœba in these dysenteries.

If the mucus be collected and freed from the contaminating feces, and be then injected into the rectum of cats, or rabbits, in

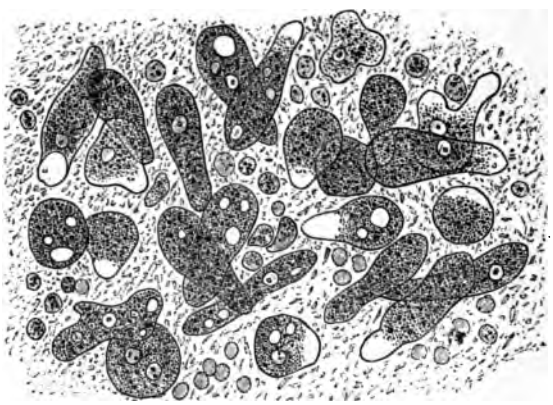
almost every instance a severe colitis is set up in the animal within a very few days, which generally runs a rapidly fatal course.

The autopsy discloses a severe ulcerative and diphtheritic dysentery, and the amœba are found deeply imbedded in the base of the ulcer. Still more conclusive is the evidence derived from the so-called amœbic abscesses of the liver, which complicate the dysentery. These abscesses are almost invariably characterized by a peculiar set of symptoms which distinguish them from those of bacterial origin. They are, as a rule, very chronic and slow in growth. They give rise to a leucocytosis which is comparatively low, ranging from 10,000 to 17,000, rarely above 20,000. They are sterile when inoculated on the media in current use, and when stained in smear reveal no bacteria. Most striking of all, is the fact that scrapings from the walls of these liver abscesses very frequently contain amœbæ, and that these scrapings, when injected into cuts per rectum, again set up an amœbic colitis. Thus the chain of circumstantial evidence is strongly in favor of an intimate pathogenic connection of the amœba with the colitis with which it is associated. A final and practical conclusion of great importance is the fact that the disease yields in a manner almost specific, and unknown in any of the bacillary infections, to the method of irrigation by quinine, a drug which exerts a peculiar, deleterious action on many rhizopods and other microzoa. The dispute could be settled finally and beyond doubt only by securing pure cultures of the amœba, and then reproducing the lesions experimentally, according to the demands of Koch's requirements. Unfortunately, this is a desideratum which cannot be accomplished, owing to the fact that the amœba does not live on our sterile media, but requires living pabulum. In view of this difficulty, the circumstantial evidence in favor of the pathogenicity of the amœba must be accepted provisorally at least, as satisfactory.

The methods of examining the feces for amœba require a certain amount of care. The stool should always be secured in a perfectly fresh condition, inasmuch as the amœbæ very rapidly die off in a stool which has been preserved over a few hours, even if the precaution be taken of keeping it at body temperature in the incubator. The fresh stool, then, is examined, and a particle of mucus, preferably streaked with blood, is selected and placed on a slide, which should be chemically clean. In adjusting the cover-glass, it is wise to insert between cover and slide a horse-hair, or some similar object, in order not to crush the organisms or interfere with their locomotion, which is their most characteristic

feature. This simple method suffices for all ordinary diagnostic purposes in most cases. In case the room in which the microscopical examination is carried on is at a temperature below 75° F., a more elaborate mechanism, known as the warm stage, must be employed in the examination. This is an apparatus manufactured by most dealers in microscopical supplies, in which a cell ground out in a glass chamber is kept at an even temperature by a continuous flow of water from a reservoir. The mechanism is very simple, and by its means the particle to be examined can be kept at body temperature for an indefinite period of time. This allows of a prolonged study of the amœba, its mode of movement, of ingestion, and its thanatology.

FIG. 85.



Amœba coli. (Mosler.)

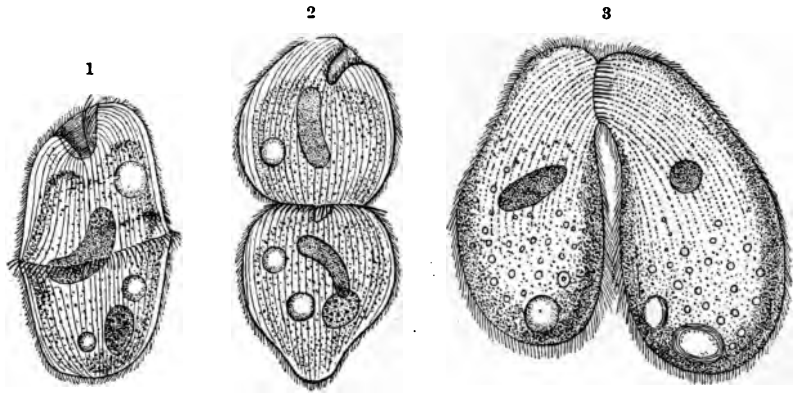
An extremely important point in the biology of the organism, namely, its mode of self-perpetuation, has, unfortunately, not yet been cleared up by the use of this method.

Under the low power of the microscope, the organisms are at once recognizable, both by their size, and by their active pseudopodial movement. They vary in size from 10 to 50 micromillimeters, the majority being far larger than the largest leucocytes or epithelial cells by which they are surrounded. In a resting condition they are rounded or ovoidal in shape, with somewhat irregular margins. In motion, they present one or more slender arm-like prolongations, "the pseudopods." As a rule, the warmer the stage, the more active is this pseudopod formation. The organism extends an arm, or process, and its protoplasm, either slowly

or with great rapidity, follows the path so laid out, and "streams" along after the pseudopod in a very characteristic fashion. The protoplasm is composed of two parts, a clear hyaline enveloping layer, of the diameter generally of less than one micromillimeter, known as the "ectosarc," and a coarsely granular interior, which makes up the vast bulk of the organism, the "endosarc." The endosarc consists apparently of a fluid matrix in which are numerous refractile coarse granules, which are, by some, supposed to represent the nodal points of a reticulum. Imbedded in the protoplasmic mass is a nucleus, which is not always distinctly to be made out. On the addition of acetic acid it becomes sharp and prominent.

In addition to these elements, which belong to the protoplasm

FIG. 86.



Balantidium coli. 1. 2, division; 3, conjugation. (After Leuckart, from Doflein.)

proper, the organism contains a large amount of ingested material, bacteria and detritus, and, in cases of dysentery, red blood cells in various stages of disintegration. It also contains numerous small, clear, rounded vesicles, the "vacuoles." Of these, a small number may be seen alternatingly to contract and expand, and are known as "pulsating vacuoles." Their function, which is not positively known, may possibly be respiratory. Spore-formation in amœba, which would offer a valuable clue in the study of the epidemiology of the disease, has been a subject of much research, with little result. Various investigators have reported encystment of the amœbæ, and endogenous spore-formation, but their results are not yet established beyond cavil.

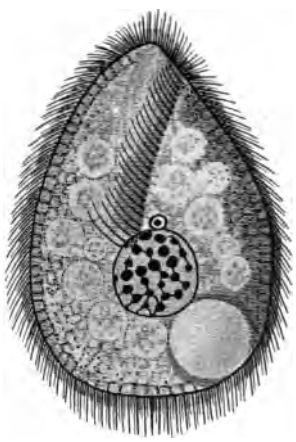
Several types of amœba have been distinguished, based upon

the degree of their pathogenicity. These are, (1) the *Amœba coli,* Loesch, (2) *Amœba coli mitis,* and (3) *Amœba intestini vulgaris.* It is, unfortunately, impossible to distinguish these forms, which are apparently essentially different from a pathogenic standpoint, by their morphological characters.

The first, *Amœba coli,* Loesch, is the true cause of dysentery, occurs in large numbers in the mucus, contains red blood cells, and is very fatal to cats.

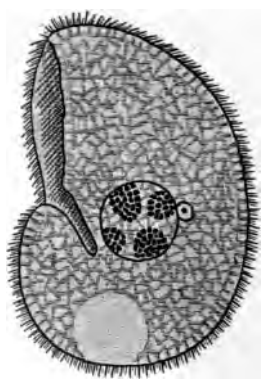
Amœba intestini vulgaris is the common and harmless symbiote which inhabits the normal gut. It occurs sparsely, except in very alkaline stools, is not associated with mucus, is harmless for cats.

FIG. 87.



Balantidium minutum.
(After Schaudinn, from Doflein.)

FIG. 88.



Nyctotherus faba.
(After Schaudinn, from Doflein.)

Amœba coli mitis is associated with certain non-dysenteric catarrhs, and is not fatal to cats. It holds a position intermediate between the two first named varieties.

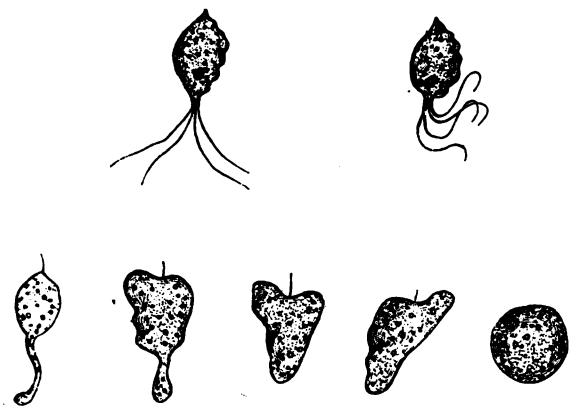
The method of injecting cats is very simple. A small part of the fluid stool, containing shreds of mucus, is injected through an ordinary small caliber catheter introduced 2 to 3 inches up the rectum. It is best then to sew up the anus of the animal for a day or two, in order to prevent the expulsion of the irritant material.

Another protozoan which seems almost certainly to stand in etiological relationship to certain forms of dysentery is the *Balantidium coli.*

Here, again, the same difficulties as in the case of the amœba

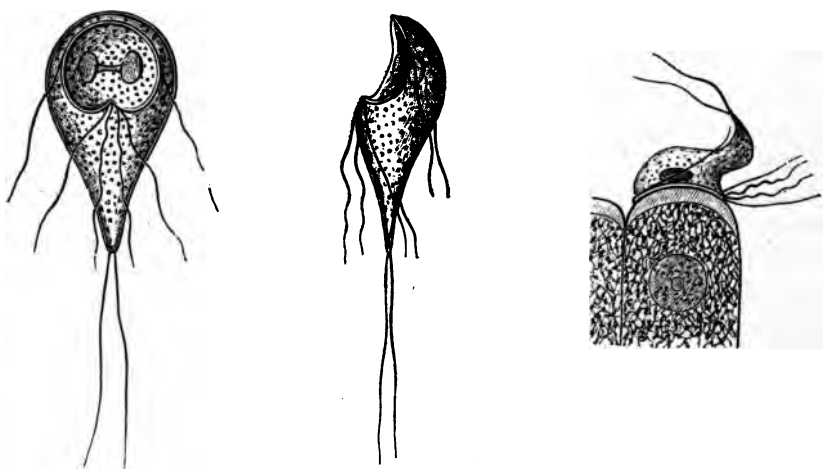
interfere with the absolute proof of the pathogenicity of the organism. The strongest argument in favor of this view is the fact that it is found deep down in the submucosa in connection with ulcers of the colon. It is an accompaniment of a very severe form of dys-

FIG. 89.



Cercomonas coli hominis. (After May, from Mosler.)

FIG. 90.



Megastoma entericum. (From Mosler.)

entery, of which the great majority of cases have been reported from Sweden and Russia.

The *Balantidium* is a normal and harmless denizen of the colon of the pig, and, it is supposed, is transferred to human beings in the process of preparing sausages.

Balantidium coli is of an oval shape, 60 to 100 micromillimeters long, 50 to 70 broad, and almost completely covered with short, rapidly vibratile ciliæ. The mouth is funnel-shaped, and surrounded by long, somewhat stiffer cilia. The anus lies at the opposite extremity. Ectosarc and endosarc are sharply separated. The latter is coarsely granular, and contains a kidney-shaped nucleus, generally two contractile vacuoles, and paraplasm in the shape of detritus, starch granules, etc. Encysted forms have been described. Motion is extremely rapid, so much so that it cannot be followed under the microscope. The organism dies very quickly, and fragments.

Other forms of doubtful interest in disease are, *Balantidium minutum*, *Nyctotherus faba*, *Coccidium hominis*, *Trichomonas intestinalis*, *Cercomonas hominis*, and *Megastoma entericum*.

WORMS.

The diagnosis of helminthiasis from the stools may be so easy as to be evident even to the laity, or it may require a considerable amount of painstaking research.

If segments of the *Tænia* pass in the stool, the diagnosis is quite patent. In other cases, suspicion of the presence of worms can be confirmed only by a thorough examination of the stools for eggs.

In the search for eggs, diarrheal stools may be examined without further preparation under the microscope. The more solid feces must be rubbed up with water, but without the use of much violence, and then examined. Where *Oxyuris* is suspected, the examination often succeeds best, if fecal matter is removed from around the anus by means of a spatula, by the introduction of the finger just within it. In this manner not only the eggs, but even the worms themselves are often removed. In case the search for eggs is fruitless, success often follows the administration of a dose of some laxative, such as castor oil. As a last resort, the diagnosis must be made ex juvantibus, by the examination of the stool after the administration of one of the vermifuges.

In case of suspected *Ascaridæ*, this procedure offers no objections, inasmuch as the therapeutic dose of santonin is usually innocuous.

The cure of *Tænia*, however, is always a serious matter, and the course should not be lightly undertaken, simply on suspicion.

It is far wiser to give a small dose of the teniafuge, say one-third of the therapeutic dose of extract of male fern, which generally suffices to drive portions of the worm out with the feces. The corroborative value of eosinophile cells and Charcot-Leyden crystals in the stool has already been mentioned in an earlier section. Eosinophilia in the blood should not be forgotten.

The worms which occur in the feces belong to three sub-orders, the *Trematodes* and *Cestodes* of the *Plathelminthes,* and the *Nematodes* of the *Nemathelminthes.*

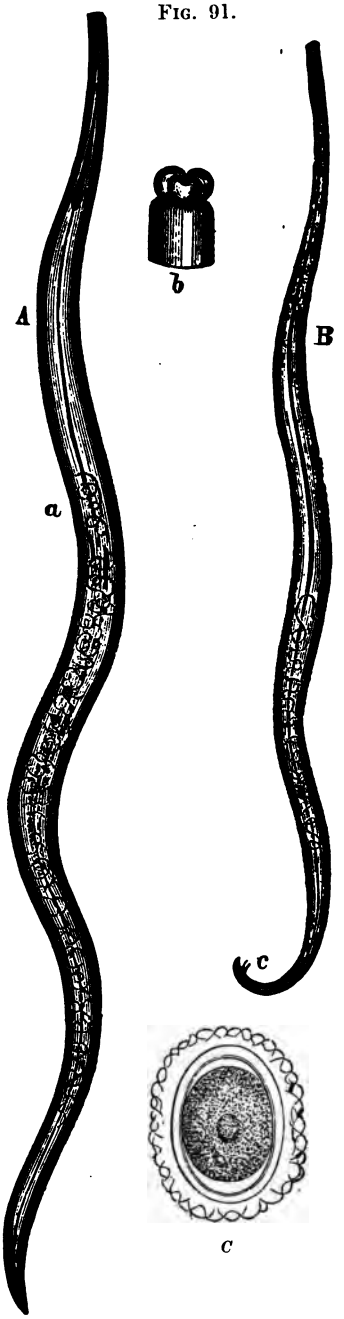
Nematodes. — The nematodes are round worms, and include the following found in human beings: *Ascaris lumbricoides, Oxyuris vermicularis, Anchylostoma (Uncinaria) duodenale, Anchylostoma (Uncinaria) Americana, Trichocephalus dispar, Trichina spiralis, Anguillula intestinalis* and *Anguillula stercoralis.*

All these worms are rounded, their bilateral symmetry being generally expressed by some external character. The sexes are distinct. There is no alternation of generations, but the mature individuals are derived in the same form from the egg. The body is unsegmented. The cuticle is thick and elastic. The mouth is terminal, and armed with "labia" which may be very hard. The gut traverses the entire body, and the anus lies near the posterior extremity.

The generative organs and their openings lie on the ventral surface. The female genital pore generally lies about midway. The male opening is conjoined with the anus. The male is generally smaller than the female. The nematodes parasitic in man are in part harmless parasites of the gut, in part very dangerous invaders which may find their way into the various viscera, and even cause death.

Ascaris lumbricoides is the most common parasite of the human intestinal canal, and often occurs as a multiple infection. These worms are found chiefly in the small intestine, but may find their way into the stomach, the bile passages, or out of the anus. The worm is cylindrical, the male ranging in length from 10-25 cm., the female from 25-40 cm. The male is easily recognized by the fact that the anal extremity is curved like a hook, and is armed with a couple of spicules of chitin. The color of the worm is a brownish-red or yellow. The oral opening is surrounded by three muscular lips which carry very fine teeth. The eggs, from which alone the diagnosis must often be made, are carried in enor-

FIG. 91.



Ascaris lumbricoides. A, female; B, male; C, egg; at *a* the female genital opening; *a*, the male spicules; *b*, the enlarged cephalic extremity, with its three lips. (After Perlo, from Ziegler.)

mous numbers by the female, and are constantly being passed off, to appear unaltered in the feces.

The eggs are 50 to 70 micromillimeters in size. They are protected by a double shell, and, outside of this, an albuminous envelope.

As it appears in the feces, the egg shows no embryo, but only a homogeneous mass of granular protoplasm, yellowish in color.

For its further development no intermediate host is necessary. The eggs may find their way to some source of water supply, and undergo further development, and may then be again taken into the stomach with the drinking water; or they may be transferred by the finger directly from anus to mouth, a mode of infection undoubtedly common among children.

If the egg still retains its albuminous envelope, it passes the stomach intact, and is only dissolved in the intestine. Here the immature egg undergoes further development, and within ten to twelve weeks arrives at sexual maturity.

The diagnosis is made from the presence of the characteristic eggs in the feces, or from the parasites themselves.

Oxyuris vermicularis, known also as the thread-worm, seat-worm, or pin-worm, is a very frequent parasite, especially in young children.

It is an inhabitant of the colon, but may crawl out of the anus at night, and into the vulva. In this way, direct infections from child to child may occur.

The worm is very minute, the male measuring 4 mm., the female 11. The female is easily distinguished. In addition to its greater length, it has a genital pore at about the middle of the ventral surface, the posterior extremity is drawn out to a point, and, when pregnant, the body is literally stuffed with eggs.

The eggs are 50 micromillimeters long, and 24 broad. They are asymmetrical, having a flat and a curved surface. They have a chitinous shell, covered by a layer of gelatinous material. The eggs are found in the feces, either as homogeneous masses of finely granular protoplasm, containing a small, clear nucleus with a nucleolus, or in various stages of embryonic development. For their further development, it is requisite that the eggs be swallowed by some animal. The gastric juice dissolves the chitinous envelope, and sets free the embryo, which then completes its development, and finds its way to the intestine. No intermediate host occurs.

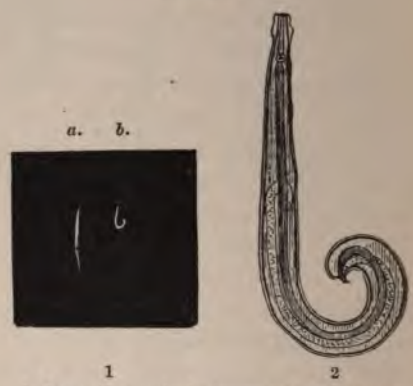
So much that is incorrect has been written about the life-history

of the worm within the intestine, and so much depends, therapeutically, on the exact understanding of these phases, that it may be well to recapitulate the newer facts. recently brought together by Heller.[1]

FIG. 92.

Oxyuris vermicularis. *a*, sexually mature female; *b*, female filled with eggs; *c*, male. Magnification, 10. (After Heller, from Ziegler.)

FIG. 93.



1. Oxyuris vermicularis; *a*, male; *b*, female; natural size. 2. Magnified.

FIG. 94.

Eggs of Oxyuris vermicularis in various stages of development. *a*, *b*, *c*, division of the yolk; *d*, tadpole-like embryo; *e*, worm-shaped embryo. Magnification, 250. (After Zenker and Heller, from Ziegler.)

Having passed the stomach and reached the intestine, the oxyuris undergoes several moults before it becomes sexually mature. Copulation between the ripe worms immediately takes place, and is probably continued in the cecum and vermiform appendix, where

[1] Deutsches Archiv. f. klinische Medicin, July 28, 1903.

it is not unusual to find a great many mature worms of both sexes. The development of the eggs begins in the fertilized female. From the cecum, the female begins gradually to trace its way along the colon towards the rectum, the development of the contained embryos meanwhile proceeding apace.

If these pregnant females be examined at the lower end of the rectum, they are found to be literally stuffed with eggs, each one containing a well-advanced organism, worm-like in shape, and capable of motility when set free from its envelope. These eggs are deposited in the rectum, and in and about the anus. They are then generally transferred by the finger to the mouth, the eggs pass on into the stomach, where the shell is dissolved, and the young embryos migrate into the small intestine.

There are thus simultaneously three broods in the intestine—the young, incompletely-developed worm in the small gut; the copulating males and females in the cecum, and the pregnant females in the colon.

Anchylostomum duodenale, also known as *Dochimus duodenalis,* or *Strongylus duodenalis,* is generally described in America as *Uncinaria.* Until a very few years ago it was generally believed that this parasite was practically limited to the Old World, occurring only sporadically in imported examples in this country. Very recently, however, it has been discovered that there are very many endemic cases both in our Southern States and in the recently-acquired island colonies.

Warfield found 80 per cent. of the schoolboys in Savannah infected, and Ashford and King report that the parasite is responsible for about one-third of the deaths occurring annually in Porto Rico.

It is, indeed, no other than the same worm which was originally described by Biermer, in Switzerland, as the agent in pernicious anemia.

There are, however, certain differences between the Old World and the American organism, which justify the erection of two distinct varieties or sub-species. The description given by Stiles, in Bulletin No. 10, Hygienic Laboratory, U. S. Public Health and Marine Hospital Service, is as follows:

"The Old World hookworm, *Uncinaria duodenalis:* Body cylindrical, somewhat attenuated anteriorly; buccal cavity, with two pairs of ventral teeth curved like hooks and one pair of dorsal teeth directed backward; dorsal rib not projecting into cavity.

Male 8 mm. to 11 mm. long; caudal bursæ, with dorso-median lobe and prominent lateral lobes united by a ventral lobe; dorsal ray divides at a point two-thirds of its length from its base, each branch being tridigitate; spicules long and slender. Female,

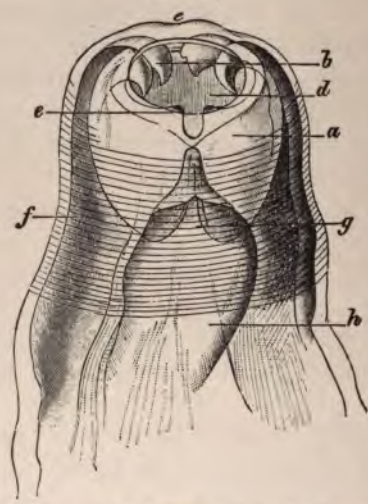
FIG. 95.

Anchylostoma duodenale, male and female. Natural size. (From Mosler.)

FIG. 96.

Eggs of Anchylostoma duodenale. *a-d*, various stages of segmentation; *e*, *f*, eggs containing embryos. Magnification, 200. (After Perroncito and Schulthess, from Ziegler.)

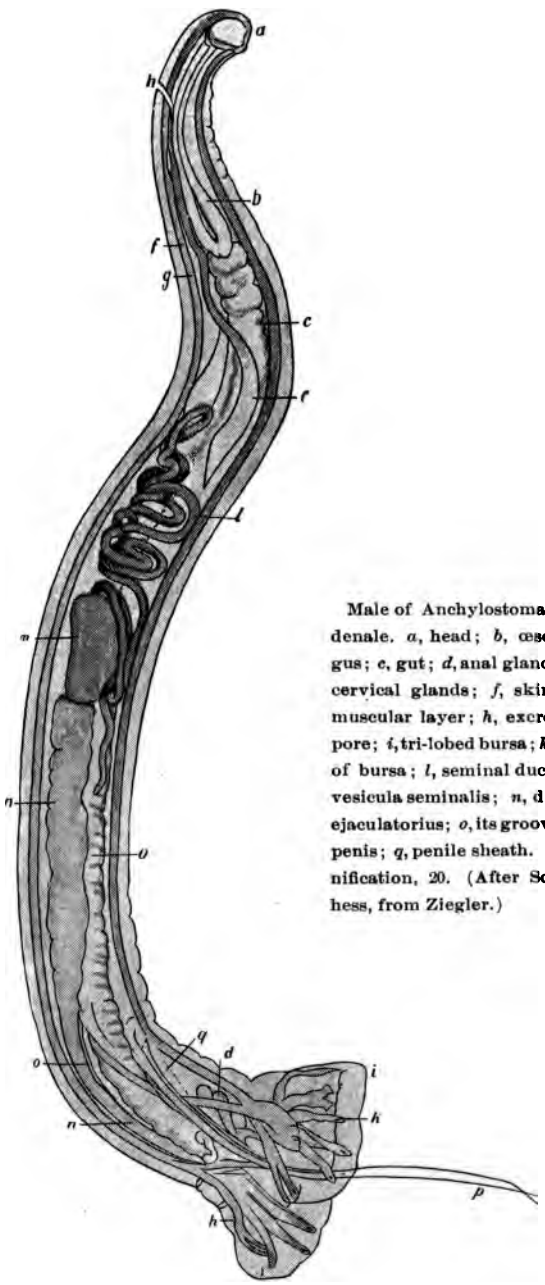
FIG. 97.



Head of Anchylostoma duodenale. *a*, buccal capsule; *b*, teeth of capsule; *c*, teeth of dorsal margin; *d*, oral cavity; *e*, ventral prominence; *f*, muscle layer; *g*, dorsal groove; *h*, œsophagus. (After Schulthess, from Ziegler.)

10 mm. to 11 mm. long; vulva at or near posteror third of body. Eggs ellipsoid, 52 micromillimeters to 60 micromillimeters by 32 micromillimeters, laid in segmentation. Development direct without intervening host.

FIG. 98.



Male of Anchylostoma duodenale. *a*, head; *b*, œsophagus; *c*, gut; *d*, anal glands; *e*, cervical glands; *f*, skin; *g*, muscular layer; *h*, excretory pore; *i*, tri-lobed bursa; *k*, ribs of bursa; *l*, seminal duct; *m*, vesicula seminalis; *n*, ductus ejaculatorius; *o*, its groove; *p*, penis; *q*, penile sheath. Magnification, 20. (After Schulthess, from Ziegler.)

"The New World hookworm, *Uncinaria Americana,* Stiles, 1902, of man: Body cylindrical, somewhat attenuated anteriorly; buccal capsule, with a dorsal pair of prominent semilunar plates or lips and a ventral pair of slightly-developed lips of a same nature; dorsal conical median tooth projects prominently into the buccal cavity. (The buccal cavity is thus markedly different from that of *U. duodenalis.)* Male, 7 mm. long; caudal bursa, with short dorso-median lobe, which often appears as if it were divided into two lobes, and with prominent lateral lobes united ventrally by an indistinct ventral lobe; common base of the dorsal and dorso-lateral rays very short; dorsal ray divided to its base, its two branches being widely divergent, and their tips being bipartite; spicules long and slender. Female, 9 to 11 mm. long; vulva in anterior half of body, but near equator (distinction from *duodenalis).*

"Eggs ellipsoid, 64 micromillimeters to 76 micromillimeters long by 36 micromillimeters to 40 micromillimeters broad, in some cases partially segmented in utero, in others (rare) containing a fully developed embryo when oviposited." The eggs of the American species are much larger than those of the Old World species.

The eggs have a transparent shell, with a linear contour. As found in the feces, they very frequently present various phases of segmentation, up to the eight-celled stage. For further development, the eggs must find their way into moist earth, where they give rise to a rhabditiform embryo. This embryo undergoes at least two moultings before it is taken into the body of its host in drinking water, or in the dirt or clay which forms so prominent a part of the diet in certain districts of the South.

In the intestinal canal, the worm completes its full development, and becomes sexually mature. It inhabits especially the jejunum and duodenum, in the mucous membrane of which it fastens itself.

The diagnosis is made by microscopical examination of the feces, in which the eggs are found, often in enormous quantities.

The feces may be strained through gauze, as recommended by Smith. It is also justifiable in suspected cases to give a full dose of thymol, after which the parasite is found in the stool as small, thread-like bodies, ½ to ¾ of an inch long, of a grayish-red color.

Strongyloides intestinalis is a worm, the presence of which in the United States was first reported by Thayer.[1] Since then several cases have been reported.

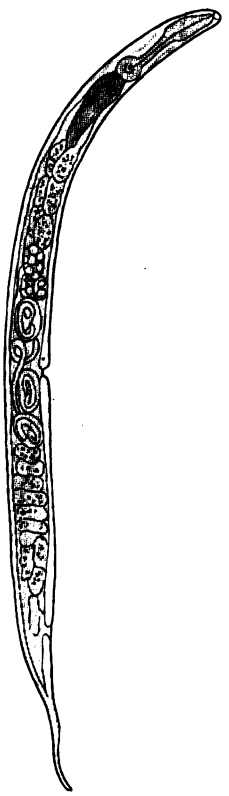
Little is known concerning the manner of infection.

[1] Journal of Experimental Medicine, November, 1901. Since then several cases have been reported.

The life-history is somewhat complicated. From the ova develop a rod-like embryo, which may further develop into the sexually distinct adult forms.

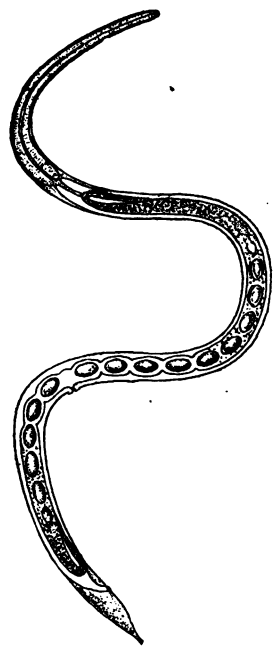
In temperate zones, however, the rod-like embryo generally passes into a thread-like stage, in which it enters the alimentary tract. Here it develops into a pathenogenetic female. The sexually

FIG. 99.



Female of Anguillula stercoralis, with eggs and embryo. (After Perroncito, from Ziegler.)

FIG. 100.



Anguillula intestinalis. (After Braun, from Ziegler.)

distinct adults copulate within the body and produce eggs which pass out in the feces, as do the eggs of the pathenogenetic form.

Different names, producing a vast amount of confusion, have been given to these various phases of the same organism. The rhabditiform embryo is known as *Strongyloides stercoralis,* or *Anguillula stercoralis;* the pathenogenetic female as *Strongyloides intestinalis,* and the mature forms which are sexually differentiated as *Rhabditis stercoralis.*

The diagnosis must be made from examination of the stool, which may contain either the rhabditiform or the filariform embryo.

The eggs are rare, and the mature forms seem not to pass out in the feces. The rhabditiform embryo occurs as a briskly-moving worm, varying from ¼ to ½ a millimeter (1-100 to 1-16000 of an inch) in size. It presents two slight ovoid enlargements of the body marked off by constrictions, and tapers to the tail.

The filariform embryo is slightly longer, and does not show the above-mentioned varieties in caliber. Forms intermediate between these two have been described. The female worm is found post-mortem.

Trichocephalus dispar, the "whip-worm," is a very widely-spread parasite. In Europe it occurs in 20 to 30 per cent. of all autopsies, but in America not so frequently.

Its pathological status is not definitely settled, but it seems probable that it is a harmless parasite.

As found at autopsies, it occupies the cecum and large intestine. It is about 5 cm. long, the male being a little shorter than the female. The shape of the worm is very characteristic; the anterior portion of the body, more than one-half of the entire length, is extremely thin, while the posterior portion, which contains the genital apparatus, is proportionally enormously thicker. In the female the posterior extremity is conical and pointed; in the male it is curved like a watch spring, and armed with a spicule. The worms themselves, although they may occur in enormous numbers within the intestinal tract, are rarely seen in the feces.

The eggs, on the contrary, furnish a frequent diagnostic evidence of the presence of the worm. They are oval, lemon-shaped, 50 micromillimeters long. They are covered by a dense, brown shell, which exhibits at each pole a small button-like projection, which is perfectly transparent. The eggs contain no embryo, only finely granular yolk. Embryonic development of the eggs, at least in the earlier stages, takes place outside of the body, in damp earth and in water. It is very slow, and even in the warm seasons occupies four or five months; in winter far longer. The embryos reach the stomach with the food or drinking water.

The *Trichina spiralis* is a worm of great importance from a pathological standpoint, which makes its sojourn in part in the intestinal canal, in part in the muscular system.

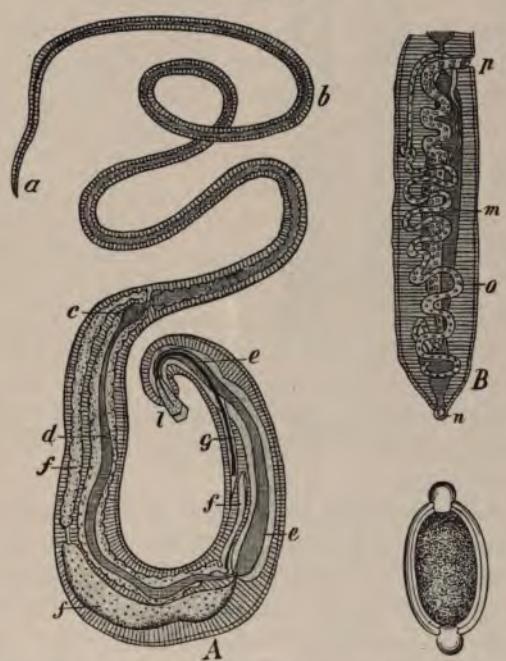
The larva, or muscle trichina, is the form in which the organism,

imbedded in the imperfectly-cooked flesh of hogs, enters the alimentary system of man. This larva is from ½ to 1 millimeter

FIG. 101.

Trichocephalus dispar. *a*, male; *b*, female. (From Mosler.)

FIG. 102.



Trichocephalus dispar. *A*, male; *B*, posterior extremity of female; *a*, head; *b*, cephalic extremity of body with œsophagus: *c*, stomach; *d*, gut; *e*, cloaca; *f*, seminal canal; *g*, penis; *l*, bell-shaped penile sheath, with tip of penis; *m*, gut of female; *n*, anus; *o*, uterus; *p*, vaginal cleft. Magnification, 10. (After Küchenmeister and Zürn. from Ziegler.)

in length, and, as a rule, lies compactly curled up within a capsule which may contain as many as two, three or five of the larvæ. In

the hog's flesh, the trichina seems to live without setting up any degree of discomfort or reactive myositis, while in man this is always very considerable, and the capsules, often even the worms, are frequently incrusted with a deposit of lime salts.

When these embryos enter the stomach of a host, the capsules are dissolved, and the intra-enteric development of the larva commences. This proceeds very rapidly, so much so that within three days the worms have, as a rule, reached sexual maturity, and begin the process of copulation. Within a week the adult female begins to give birth to embryos, and continues to pass them out for several weeks, during which period, it is asserted, between 1,000 and 2,000 are born. The embryos are supposed to be deposited in the chyle vessels in the wall of the intestine, whence they migrate to the various muscles of the body, and recommence the cycle.

The diagnosis may occasionally be made by finding the mature intestinal form or embryos in the feces, though this is, indeed, a rare occurrence. The adult form measures 3 to 4 mm. in the female, and is just appreciable by the naked eye. The male is 1 to 2 mm. long, and has two conical projections from the anal extremity. The embryo is only 1 mm. or less in length. Eosinophilia is a constant accompaniment of the presence of trichina.

The Cestode Worms.—The cestodes, known popularly as Tape-worms, are distinguished both by their external form, and by their biological relationship to their hosts from the round worms.

Externally, they are long, flattened, segmented worms. The first member of the segmented series, known also as head and as "scolex," is specialized in such a manner as to fit it for maintaining a hold on the intestinal canal of its host. It has suckers, and, in addition, in some species, a circlet of hooks. This head is derived from an embryo contained in the ingested flesh of various domestic animals which are used as food.

By asexual generation, or budding, it gives rise to all of the succeeding segments, the youngest of which is, of course, that nearest the head. These successive segments are morphologically exactly similar, but diminish in size toward the head. They are known as proglottides. The embryo is called a cysticercus. The cestodes parasitic in man belong to the families of the *Tæniadæ* and the *Bothriocephalidæ*. The former occur in man either as cysticercus or as tape-worm; the latter only as tape-worm.

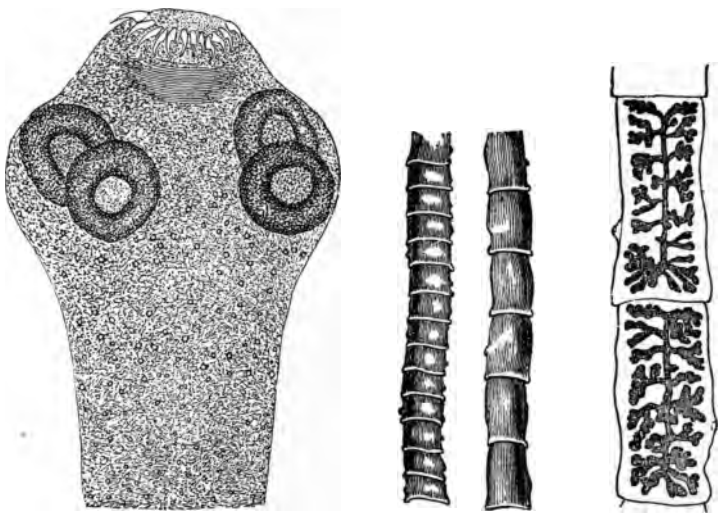
Tænia Solium, a worm which was once very common, owing to a custom, formerly more prevalent, of eating raw ham, is now

seldom seen. In Germany, too, the worm has been well nigh exterminated in certain districts through the Government supervision of swine's meat.

It is a strange fact, however, that the cysticercus form continues to occur with disproportionate frequency (Marchand).

The tape-worm attains a length very often of three meters. The head is smaller than the head of a pin. Examined under the microscope it appears to be pear-shaped, and is armed with four lateral prominent suckers and a circlet, or rostellam, of hooks at

FIG. 103.



1, Head of Tænia solium; magnification, 50; 2, 3, Mature and semi-mature segments, natural size; 4, Two proglottides with uterus, twice magnified. (From Ziegler, after Leuckart.)

its crown. These hooklets are 26 in number, short and broad, and provided with a lateral spur. Below the suckers, the head becomes narrowed, and is prolonged into a slender "neck." The hooks and suckers serve as organs of fixation whereby the parasite anchors itself to the intestinal wall. Below the neck, the immediate proglottides are narrow and elongated, and gradually become broader and less long as they approach the other extremity of the worm. The mature proglottides are found at a distance of 100 to 150 cm. from the head. They are about 10 mm. long and 6 to 7 broad. Externally, slightly behind the middle of the lateral surface, is a papilla which contains the genital orifice or pore. Into this

empty the canals both of the male and female sexual apparatus, for each proglottis is hermaphroditic. The male generative organ, or "testis," is represented by a number of clear vesicles scattered throughout the segment, which unite by means of a system of branched canals to empty into the vas deferens. The "ovary" consists of a series of interconnecting tubules which form a sort of arborization. This again voids to the exterior by the "vagina," which opens into the common cloaca at the genital pore. Through the middle of the proglottis runs the broad uterus, with many branched lateral processes. In this organ the eggs attain their development. Laterally lie two canalicular systems, which are a means of communication between the successive segments, namely, the excretory and the water vascular systems. Externally, the proglottis presents a muscular layer of smooth muscle fibers, amongst which are interspersed many of the so-called calcium corpuscles.

The eggs may be found in the various segments in all stages, from that of the unfertilized ovarian egg to the embryo contained in the uterus. The ovarian eggs are light yellow, rounded bodies without a cuticle.

The progressive development of the egg is marked by the acquisition of yelk, and of a thick, brownish, chitinous envelope. In the uterus segmentation takes place, with the development of an embryo possessing a rudimentary scolex with six hooklets. In this form, the eggs leave the body, and eventually enter the stomach of their new host, where the cuticular shell is dissolved. The embryos then bore their way through the intestinal wall and become imbedded as a "cysticercus" in the organs.

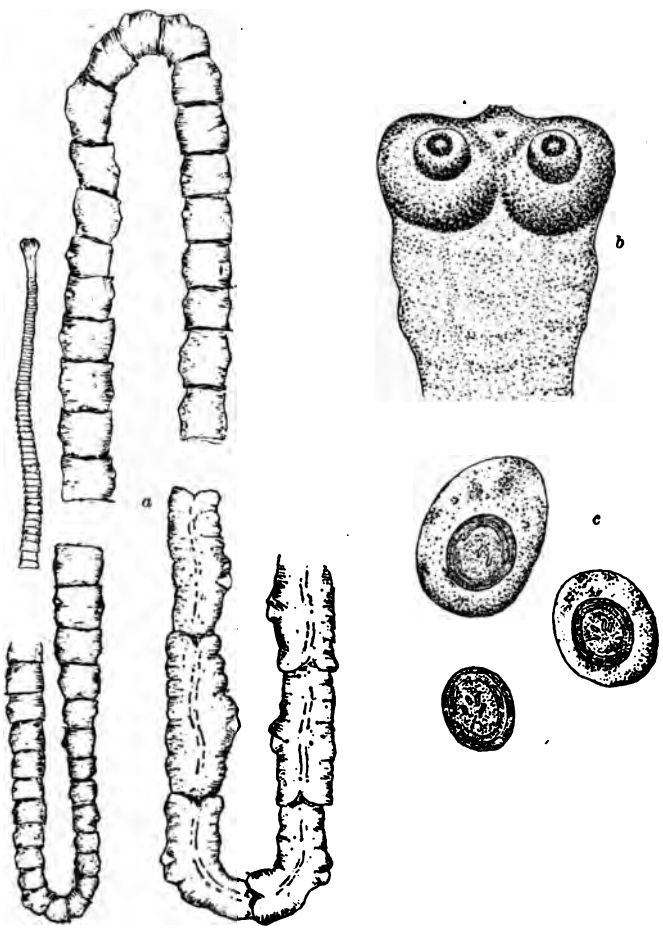
As has been said, the cysticercus is occasionally found in man. *Tænia saginata,* the most frequent form of tape-worm met with in America, is found as a cysticercus in so-called "measly beef." When this is eaten raw, or insufficiently cooked, the embryo develops into a tape-worm in man.

The cysticercus of *Tænia saginata* is found in human beings only as a very great rarity.

The worm, when full grown, attains a considerably larger size than does *T. solium.* It measures in length as much as 4 to 7 meters, and the proglottides are severally larger and broader than those of *T. solium.* The head has a flat crown, and no rostellum. It is armed with four powerful suckers, which have a pigmented border. The uterus possesses a vastly greater number of lateral processes

than does that of solium, and they present instead of the terminal arborizations seen in the latter form, only dichotomous divisions. The sexual pore is situated on the lateral margin, slightly behind the middle of the body. The eggs are indistinguishable from those of *T. solium,* and undergo a similar development.

FIG. 104.



Tænia saginata. (Simon.) *a*, natural size; *b*, much enlarged; *c*, ova much enlarged.

Tænia cucumerina (see *elliptica)* is 15 to 20 cm. long. The head possesses a rostellum. It occurs in dogs and cats, rarely in man.

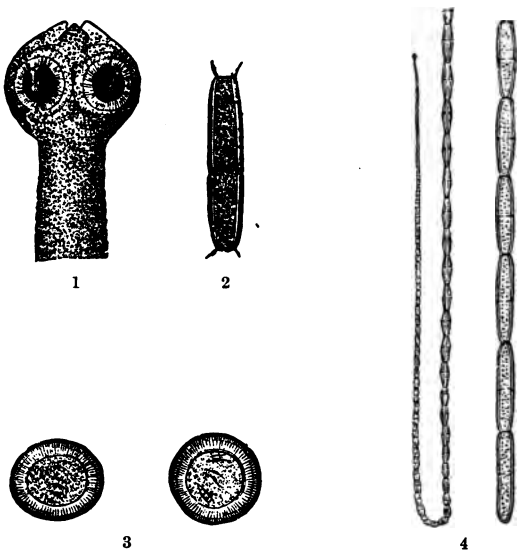
The cysticercoid is parasitic in the flea of the dog, rarely in the

pediculi which infest human beings. The cysticercoid occurs in cattle.

Tænia nana (Hymenolepsis nana) occurs not infrequently in southern Italy, and rarely in other parts of Europe. In the United States attention has been paid to the worm only of late years. About 20 cases have been described, the majority of them in the Southern States.

The worm is 8 to 15 mm. in length, and its diminutive size is probably responsible for its having so rarely been discovered. It occurs in vast numbers, usually located in the lower part of the ileum. It has four stickers, and a crown of hooklets. Each segment possesses three testicles, a generic characteristic. The genital pores are situated on the left lateral margin.

FIG. 105.



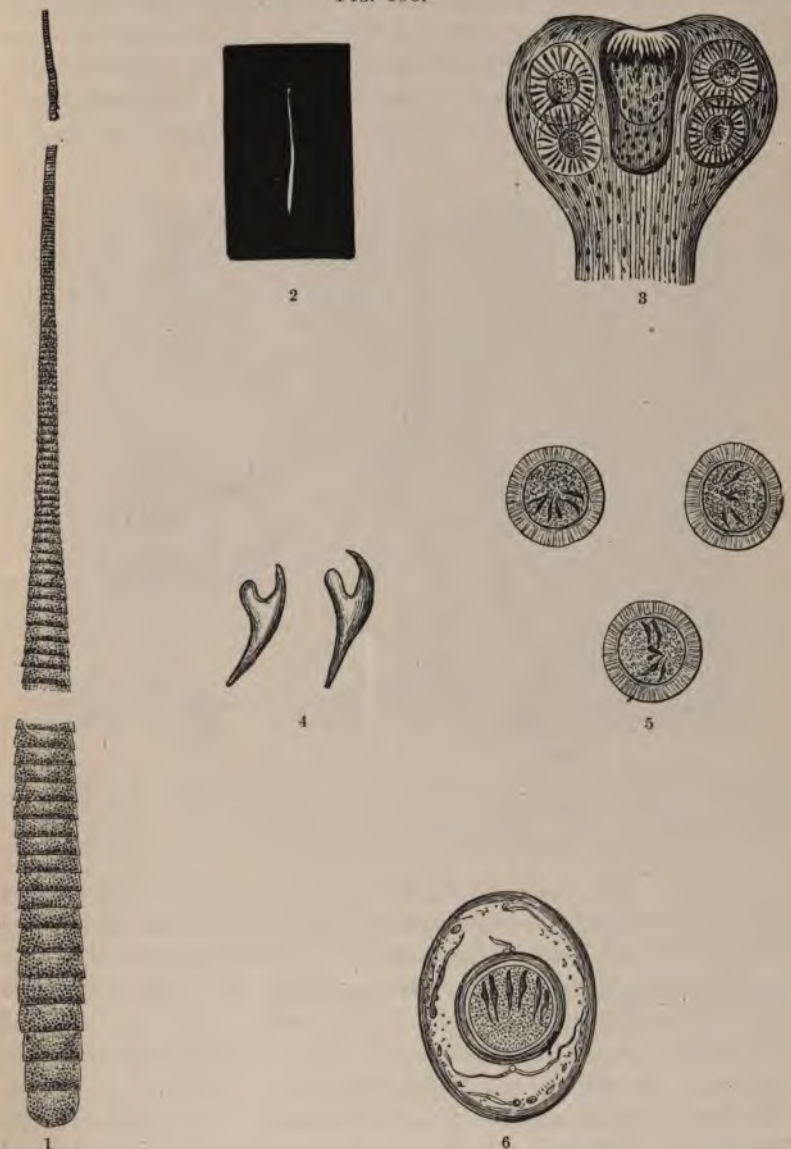
Tænia cucumerina. 1, head; 2, mature proglottis; 3, eggs; 4, segments.

The eggs have two distinct membranes, "the inner one presenting at each pole a more or less conspicuous mamillate projection provided with filamentous projections."

The entire life-cycle of this form seems to be followed within the intestinal tract of man, the eggs developing in the intestinal villi. Infection probably occurs from man to man through the medium of hands soiled with infected feces. Infection may persist for years.

The diagnosis is most readily made by microscopical examination of the stools for eggs. The worms are so minute as generally to escape macroscopic detection.

FIG. 106.

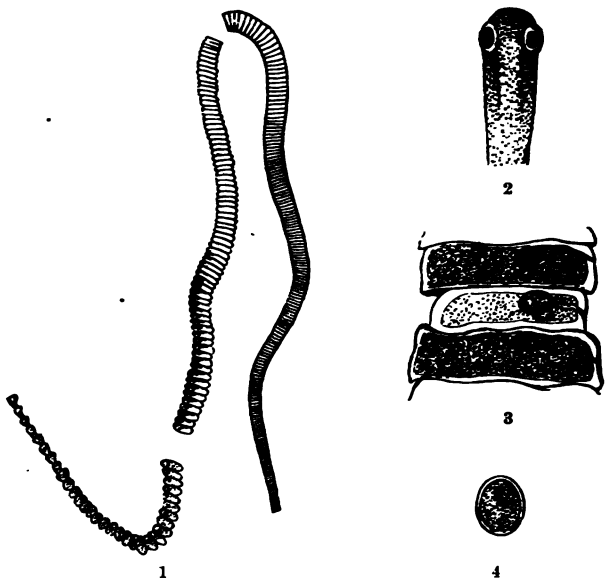


Tænia nana. 1, body; 2, natural size; 3, head; 4, hooklets; 5, eggs; 6, egg, magnified 600 times. (From Mosler.)

The method recommended by Hallock[1] for finding the worms is as follows:

"The method which so far has proved most satisfactory in finding the parasites is to dilute the stool with considerable quantity of water, and then to run it out in a very thin layer on a large plate of window glass having a black background and placed in a strong light, the examination being made with a large reading glass. The worms appear as very minute translucent or opalescent shreds not unlike mucus, and the greatest care is required lest they be

FIG. 107.



1, Tænia flavopunctata; 2, head; 3, mature proglottides; 4, egg. (From Mosler, after Weinland.)

overlooked. The ova are found with the microscope much more easily than the worms themselves, a two-thirds objective being ample after one becomes familiar with their appearance. The spread should be very thin, and but little light admitted from the condenser."

Considerable clinical significance attaches to these worms, inasmuch as in the cases in which they were detected they were responsible for abdominal and reflex nervous symptoms of some severity. Attention has been called to the fact that the undigested portions of bananas may simulate small tape-worms.

[1] Journ. Am. Med. Association, April 2, 1904.

Hymenolepsis (or *Tænia) diminuta* (or *flavopunctata)* is a tape-worm 20 to 60 mm. in length, which occurs frequently in rats and mice, but very rarely in man. The head has no hooklets. The cysticercoid is said (Grassi) to inhabit a small butterfly.

Tænia Africana (Linston) is a recently-described species found in the negroes of Dutch East Africa.

Tænia confusa, a new species described by Ward.

Bothriocephalus latus (Bremser) is the largest of the

FIG. 108.

Middle piece of a proglottis of Bothriocephalus latus, seen from the dorsal surface; the external layer almost completely removed; *a*, lateral vessels; *b*, seminal vesicles; *c*, seminal ducts; *d*, vas deferens; *g*, generative glands; *h*, yolk chambers lying in the cortical layers; *i*, collecting tubules of yolk chambers; *l*, commencement of uterus; *m*, coils of the uterus filled with eggs; *n*, vagina; *o*, vaginal opening.

human tape-worms, reaching a length of 5 to 8 meters, and consisting of as many as 3,000 to 4,000 short segments.

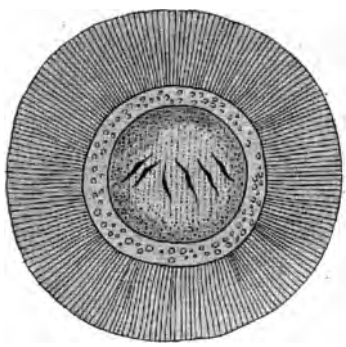
The body of the worm differs from that of the tænia previously described, in that it tapers towards both extremities. The centrally-situated segments, which are the largest, measure 3.5 mm. in length, 10 to 12 in breadth. The head is ovoid, 25 mm. in length, and 1.0 mm. broad, somewhat flattened, and provided on each lateral aspect with a groove-like sucking apparatus. The uterus is a simple, slightly-convoluted canal. The sexual openings lie in the

middle line on the ventral surface, the female pore behind the male.

The eggs are ovoid in form, 0.07 mm. in length, 0.045 mm. in breadth. They possess a thin, brown capsule, of which the anterior pole presents a very distinct and remarkable cap.

The worm occurs in Switzerland, Holland, northeastern Europe and Japan. It is said to occur in America only as an imported disease. It may exist as a harmless parasite, or may occasion fatal anemias. The plerocercoid inhabits certain fish, the ingestion of which frees the embryo which develops into the tape-worm in man. In this form it inhabits the small intestine. At long intervals, segments are passed off in the stools, generally owing to some

FIG. 109.



Free embryo of Bothriocephalus latus, with ciliæ. (After Leuckart, from Ziegler.)

FIG. 110.

Eggs of Bothriocephalus latus; the one to the right after the discharge of yolk. (After Leuckart, from Ziegler.)

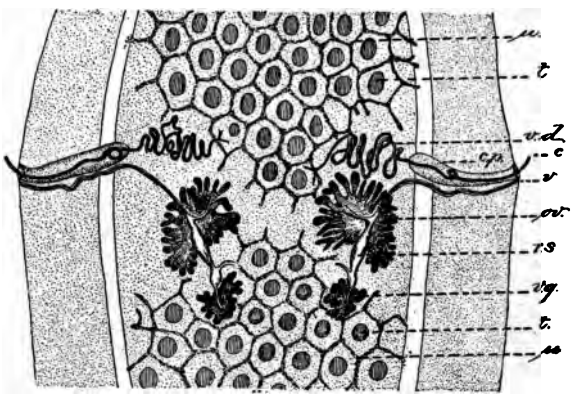
change in diet. The diagnosis may be made by finding these, or eggs in the feces.

Bothriocephalus cordatus is a tape-worm of 80 to 120 cm. length. The ripe proglottides measure 7 to 8 mm. in breadth, 3 to 4 in length. It is rarely found in Greenland and Iceland in man, more frequently in dogs. The intermediate host is a fish.

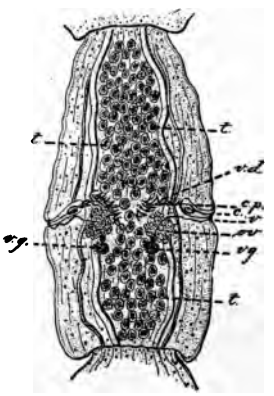
Dipylidium caninum. This is a very common parasite in dogs and cats, and has been found in very rare instances in human beings. The parasite belongs to the family *Tæniidæ,* sub-family *Dipylidiinæ.* The description, as taken from Stiles, is as follows: "Suckers unarmed. Rostellum armed, rarely absent. Genital pores lateral, single, or double, and opposite. Genital organs of each segment in single or double series. Uterus usually divides

FIG. 111.

1



2

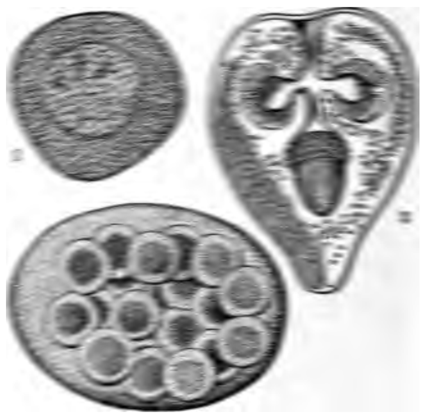


3

1, Adult strobila of Dipylidium caninum (Stiles). 2, Mature segment of same (Stiles). 3, Gravid segment. *c*, cirrus (penis); *c.p.*, cirrus pouch; *ov.*, ovary; *r.s.*, receptaculum seminis; *t*, testicle; *u*, uterus; *v*, vagina: *v.d.*, vas deferens; *v.g.*, vitellogene gland. (From Stiles, after Diamare.)

[illegible]

[illegible]



1. Egg packets of Dipylidium.
2. Egg of same enlarged. After Stiles.
3. [illegible] larval stages of Dipylidium, as found in the flea. After Leuckart.

[illegible]

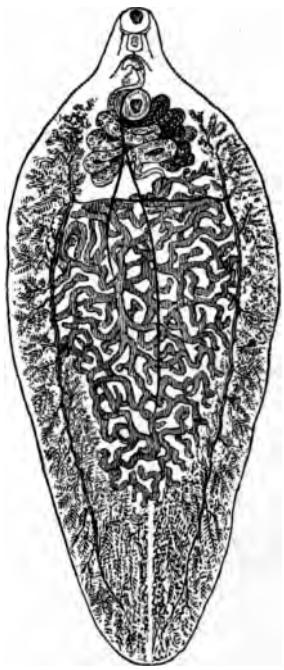
[illegible] hepaticum, magnification [illegible]. (From Ziegler, after Leuckart.)

Other worms of less moment are:

Trematoda Worms. Of these worms only rare examples have been found in the fæces, belonging to the species *Distoma hepaticum*, and *Distoma lanceolatum*. They are apparently without pathological significance. *Distoma buskii* has been found in

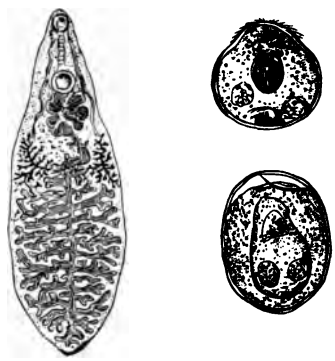
China. Oysters serve as a host. *Distoma sibiricum, Distoma spatulatum,* and *Distoma conjunctum* are other rare trematodes occasionally found in man.

FIG. 115.



Distoma hepaticum, with male and female genital apparatus. (From Ziegler, after Leuckart.)

FIG. 116.



Distoma lanceolatum. (v. Jaksch.)

CHAPTER XVIII.

CHEMICAL EXAMINATION OF FECES.

Under the heading of chemical examination of the feces will be included those other methods belonging to the physical sciences, including spectroscopy, which have for their object a quantitative determination of certain conditions.

A considerable amount of labor has been bestowed on this branch of coprology, but not as yet with corresponding practical results for the clinician.

Of most value are the purely qualitative reactions, as for the determination of the presence of blood. The feces represent the end result of such a complex series of processes that quantitative examinations, of the gross kind which we are at present in a position to employ, fail of their object. They give us exact figures, but no accurate clinical information.

Methods.—To a certain extent we can introduce at least one positive factor into our calculations from the end result represented by the stool. This is offered by the diet. In order to supply a constant datum for comparison, Schmidt has suggested the following "test diet," which represents a normal mixed diet: 1½ liters of milk, 3½ eggs, gruel from 80 grammes of oatmeal, 100 grammes zwieback, 20 grammes sugar, 20 grammes butter, 125 grammes fillet, raw; 190 grammes potatoes, raw; together about 126.25 grammes of albumin, 83.4 grammes of fat, and 218.5 grammes of carbohydrates, which are equivalent in all to 2,183 grammes calories.

They suggest the following subdivision of this diet:

6.30 A. M.—⅜ liter milk, 2 zwieback.

9.30 A. M.—⅜ liter milk, bouillon, with ½ egg.

11.00 A. M.—⅜ liter milk, 1 egg.

12.00 M.—½ liter oatmeal gruel (from 40 grammes oatmeal, 166 grammes milk, 10 grammes sugar, and ½ egg), 100 grammes boiled chopped meat (from 125 grammes raw beef and 12 grammes of butter), 250 grammes potato purée (from 190 grammes mashed potatoes, 60 grammes milk, 8 grammes butter).

3.30 P. M.—⅜ liter milk, 1 egg, 1 zwieback.

6.30 P. M.—½ liter oatmeal gruel.

This diet may be modified by the omission of the beef and the potatoes at noon.

This diet seems to be well borne by most patients, and may be continued for days. If the milk at first sets up a diarrhea, this generally subsides within a short time.

It is often advisable to mark off in some manner the beginning and end of the use of some prescribed form of diet in such a way as to render its appearance evident in the feces. This is the more necessary, inasmuch as the feces, even with daily evacuations, does not always contain the remains of the diet of the preceding day. Ranke used cranberries for this purpose, but they are not always tolerated by the gut, nor reliable. Rubner used emulsions of carbon, which have since been generally adopted (Carbo. veg., 15.0; mucilage gummi arab., 15.0; ag. menth. pip., 60.0; three dessertspoonsful). Patients with digestive disturbances do not tolerate such large quantities of indigestible material, and in such cases it is wiser to substitute carmine for the carbon. Schmidt marks off his test-diet by giving at the beginning and the end, 0.3 grammes of finely-powdered carmine in a wafer. The method is not applicable in case one wishes to make the blood test as subsequently described, because the coloring matter of the carmine interferes with the color reaction.

It is customary to do chemical examinations on the dried feces. The drying may be carried on over a water-bath at low temperatures. The loss of nitrogen consequent on this method may be prevented by the addition of a little sulphuric acid.

The method of procedure in a chemical analysis is, of course, largely dictated by the special object in view. The weight, reaction, dry residue, are first to be determined. The watery extracts contain part of the coloring matters, soluble albuminates, peptones, ferments, a few volatile fatty acids, sugar, and part of the salts. If the feces are diluted with water and slightly acidified with mineral acids, the distillate contains volatile fatty acids, phenol, indol, skatol, alcohol, acetone and H_2S.

If the acidified feces are extracted first with alcohol and then with ether, one obtains the fats (free fatty acid, neutral fats), lactic acids, cholesterin, lecithin, blood pigments, biliary pigments, sugar, part of the salts, glycosides, chlorophyllan, leucin, tyrosin and diamine.

In the residue remain keratin, elastin, nuclein, cellulose, amylum, dextrin, gums.

Reaction.—The customary manner of making a qualitative test of the reaction of the feces is to moisten pieces of red and blue litmus paper with distilled water, and then to touch them with particles of the feces.

A better method, as suggested by Krauss, is to introduce a few cc. of a watery solution of litmus tincture (1-10 of water) into each of a couple of test-tubes of equal diameter. To one of these a small amount of the fecal matter is then added, and the reaction determined by a comparison of the color. In case the test-tubes become clouded through the addition of the feces, this difficulty may be obviated by centrifugation.

The test should always be made on freshly-passed feces, inasmuch as the reaction may subsequently change quite rapidly to alkaline or acid. The entire fecal mass should also be well mixed, as it may vary in reaction in different parts, and if it be inspissated and scybalous, it should be rubbed up with distilled water.

If one desires to test the reaction with a variety of indicators, it is always well to prepare a watery extract with distilled water, which is then filtered. In this manner, minute differences in reaction are occasionally brought to light, owing to the varying susceptibility of the indicators. A neutral reaction to litmus may be faintly acid to phenolphthalein, and alkaline to cochineal. For all clinical purposes, the litmus reaction suffices.

The quantitative test is made with phenolphthalein as an indicator, and titration is performed either with one-tenth normal soda, or one-tenth normal hydrochloric acid.

Twenty to fifty grammes of fresh feces are rubbed up with 10 times their volume of distilled water in a mortar. Titration is now performed, and the result controlled either with phenolphthalein, or by repeatedly testing the reaction with litmus paper. In the former case, the reaction is complete when the red color remains permanent; in the latter when a light bluish halo surrounds the test-drop. The reckoning is then made on a basis of 100 grammes of feces.

The reaction of the feces is ordinarily neutral or slightly alkaline. If strongly alkaline, the reaction is probably due to an excess of ammonia generated by putrefaction of the nitrogenous elements.

If strongly acid, the reaction is determined by the presence of free fatty acids, both the volatile and the higher acids. The former, with lactic acid, are due to the predominance of carbohydrate decomposition, the latter to a superfluous quantity of fat in the

feces. The fixed alkalies and mineral acids, even though they occur in considerable amounts, rarely affect the reaction. The excess of alkali in the ash is generally bound by organic acids.

Thus it becomes evident that carbohydrate fermentation, or the splitting of fats, determines an acid reaction, while the putrefaction of the proteid elements makes for an alkaline reaction in the stools. As a rule, the form of diet is, therefore, of significance in the final result.

The feces of nurslings reared on mother's milk is acid. In case artificial feeding is used, especially with dilution of the milk with gruels, the reaction is neutral or faintly alkaline. Meat or milk diet in adults yields a neutral or alkaline feces.

The reaction is also influenced by the condition of the digestive tract. If bile be lacking, as in closure of the common duct, the reaction is acid, owing to decomposition of the fats. Pancreatic diseases and disturbances of the absorptive function likewise favor decomposition, and determine an acid or alkaline reaction depending on the nature of the diet.

The diagnostic significance of the reaction of the feces is slight. In cases of infants an accentuation of the normal acid reaction points to fermentation. Acidity occurs in the feces of infants, combined with greenish discoloration, and a butyric acid odor, in cases of simple dyspepsia, and at the beginning of most acute illnesses. At the height of these diseases, enteritis, enteritis tuberculosa, tabes mesaraica, typhoid, etc., the reaction is almost invariably alkaline, and the odor generally ammoniacal. Among adults, the value of the reaction is much less limited.

Dry Residue.—The determination of the dry residue of feces affords a scientific measure of the terms diarrhea and constipation. Although quantitative determinations have not as yet proved of greater diagnostic value than the simple macroscopic estimate, it is highly probable that they will play a larger rôle in the coprology of the future.

The method of arriving at a quantitative estimate of the solid contents of feces is simple. The stool is first evaporated to dryness over a water-bath. This process may be hastened, and the evaporation point at the same time lowered by the addition of small quantities of alcohol. In order to prevent the evaporation of NH_3, which would subsequently effect the quantitative nitrogen determinations, it is customary first to determine the reaction of the feces, and if alkaline, to add a small amount of dilute sul-

phuric acid. If the feces are very rich in fats, drying over a water-bath tends to reduce the mass to very adherent clumps, which interferes with the subsequent process of pulverisation. It is wise, therefore, to avoid this difficulty by drying the feces over heated sand, the weight of which has been previously ascertained. The second step of the process consists in driving off the last remnants of water by means of the hot-air desiccator. In order to accomplish this, the feces must first be pulverized, or, if fatty, rubbed up with sand. Desiccation is done at a temperature of 105° C., until the stools have reached a constant weight. Fatty stools must be kept at a lower temperature (97 to 99° C.), inasmuch as the fats would otherwise form an impermeable layer over the surface of the fecal mass. To offset the lower temperature, the process must be continued over a longer period, even as much as two days.

The details of the entire procedure are as follows: A given quantity of fecal matter is weighed, and then dried, first over the water-bath, then in hot-air apparatus, until its weight has become constant. The final weight, as compared with the first, gives the percentage of solid constituents.

The percentage of solid residue must naturally vary largely with the nature of the diet. A meat diet leaves a far smaller residue of solids than does a vegetable diet. These differences, under normal circumstances, may run from 15 to 35 per cent. The residue, after various forms of diet under normal conditions, has been carefully estimated, and is presented in the following table by Schmidt and Strasburger:

DIET		DRY RESIDUE	AUTHORS
1. Meconium		20	Zweifel.
2. Starvation	Dog	20-40	Zweifel.
3. Milk	Man	12-13	Müller.
a. Infants	Mother's	15	Uffelmann.
	Cow's	15-25	Biedert.
b. Adults	With additions	15-20	Uffelmann.
	Pure	28	Uffelmann.
4. Meat	Dog	34	Müller.
	Man	29	Müller.
5. Meat and Fat		27.5	Rubner.
6. White bread		25	Rubner.
Nudels, etc.		. . .	Rubner.
7. Black bread		15	Rubner.
8. Potatoes		15	Rubner.
9. Peas		13.4	Rubner.
11. Mixed		26	Voit.

It is not a simple matter to explain the increased amount of water in the stools of a vegetable diet. Rubner ascribes it to the acidification of the intestinal contents, which tends to inhibit the absorption of water. On the other hand, diets, such as meat and milk, which have a constipating effect, naturally produce scybalous and desiccated feces. There are, of course, other factors which even in health influence the amount of water in the stools, *e. g.*, deficiency in the amount which is ingested, great loss of fluids through sweating, and so forth.

Conditions of disease both within and without the intestinal canal largely influence the consistency of the fecal mass. Constipation is the most physiological, if it may be so termed, and the most constant cause of an alteration of the normal balance. The feces become hard, and their water may be reduced as low as 60 per cent. In diarrheas, on the other hand, the percentage of water rises appreciably, as in most diseases of the intestine. In cholera, the stools contain 98 to 99 per cent. of water.

It is essential in making estimates of this kind to employ a definite form of diet of which the normal average residue is known. With the test-diet of Schmidt, as previously described, the dry residue has been found to amount to 24.25 per cent., and to vary with pathological conditions, such as dyspepsia and acholia.

Increased proportion of the solids in the stools is primarily due to diminished peristalsis, which, again, is a symptom of a considerable number of intestinal diseases. Increase of the water may be due either to diminished absorption of water, or to increased elimination from the wall of the gut. The former is a factor chiefly in cases with increased peristaltic action from any cause, whether due to the nature of the intestinal contents, inflammatory, or nervous. But diminished absorption capacity may also be a characteristic of certain diseases of the intestinal mucosa, *e. g.*, atrophy, and amyloidosis. Increased exudation or transudation of fluid from the intestinal wall occurs in many catarrhal and inflammatory conditions, mixed in varying proportions with pus, blood, or other solid constituents.

Total Nitrogen.

In making the test for nitrogen in the feces, the method of Kjeldahl, already described in connection with the urine, is employed. The nitrates are lost by this method, but are of no account, inasmuch as they occur in such small quantities as to be a negligible factor. The details of the method as applied to the analysis

of the feces by Schmidt and Strasburger are as follows: One takes two portions, each of 2 to 4 grammes of fresh feces, or of 0.5 to 1 gramme of feces which have been dried with the addition of sulphuric acid, as previously described. Each of these is placed in a Kjeldahl flask, together with 20 cc. of sulphuric acid mixture, and one drop of metallic mercury. The so-called sulphuric acid mixture is composed either of three parts of pure concentrated plus one part of fuming sulphuric acid, or of 800 cc. pure, 200 cc. fuming sulphuric, and 100 grammes of anhydrous phosphoric acid. It should contain no free nitrogen. The mercury can be washed free of all traces of nitric acid, and is best dropped from a capillary pipette. This mixture is well shaken, and set aside for twelve to twenty-four hours. The tube is then heated on a sand bath for three to four hours, first with a small, then with the full flame, until the fluid becomes perfectly clear and transparent. The flask is then held in a bowl of cold water, and to its contents are gradually added 50 cc. of distilled water. The whole amount is then poured into a retort, which is cooled by water from the hydrant, and to it are added enough soda to alkalinize, and 40 cc. of potassium sulphate (40 grammes : 1l), also a few zinc filings.

The retort is now connected with the condenser, and distillation begun. The nitrogen bulb into which the ammonia is received should contain 40 to 50 cc. (measured) of one-fifth normal solution of sulphuric acid. Distillation should be completed in twenty minutes, when the cork of the flask is removed, and the distillate titrated. This is done with one-fifth normal soda solution, using cochineal as an indicator. The calculation is made by multiplying by 2.8 the number of cc. of one-fifth normal soda bound by NH_3; the latter figure is obtained by subtracting from the total number of cc. of soda used in titration, the number of cc. of sulphuric acid solution previously added to the mixture..

The sources of nitrogen in the body are, (1) the secretions and other contributions (desquamated cells, etc.) of the body; (2) the bacteria and their products; (3) the proteids of the food. The first two factors, as has been previously shown, cannot be determined with any degree of exactness in health, inasmuch as the analysis of the feces in starvation gives figures which can only distantly approximate those which maintain under normal conditions.

On an average it has been found that "starvation feces" contain 0.254 grammes of nitrogen. On a nitrogen free diet, Rieder found that 0.73 grammes of nitrogen were excreted daily. This

shows conclusively that the amount of food influences the amount of nitrogen directly contributed by the body to the feces. Rieder estimates that this constituent, on a mixed diet, amounts to 29 per cent. of the entire amount of nitrogen in the feces. The increase in the nitrogen contributed by the body on a full diet is partly due to increased secretion, partly to increased desquamation, and largely to an increase in the number of bacteria.

The food determines to a great degree the nitrogen contents of the feces. The quality of the food, its quantity, and the thoroughness with which it is digested, are all important factors in the final result. As regards the quality, it is a generally valid rule that the more "digestible" a food, *i. e.*, the less it leaves of solid residue, the less nitrogen does it contribute to the feces.

To mention only the more important articles of diet, meat, if well prepared, eggs, milk, and certain few vegetable foods, such as rice, white-bread, nudels, leave little residue, hence little nitrogen, while, on the other hand, a diet rich in vegetable (cellulose) constituents, increases the nitrogen content of the feces very considerably. An important consideration is the fact that the percentage of nitrogen to the entire residue does not necessarily rise with the increase of the total nitrogen; in fact, the reverse maintains. This is an apparent contradiction which is very easily explained. The indigestible foods, while they contribute a considerable amount of undigested proteids to the feces, thus increasing the total nitrogen, contribute far more, proportionally, of other constituents, so that the percentage of nitrogen actually sinks, while its total quantity rises. This is well indicated by the following tables, taken from Schmidt and Strasburger:

DIET.	GRAMMES.	DAILY NITROGEN. GRAMMES.	PER CENT. OF DRY RESIDUE.
1. Macaroni	6.95	1.86	6.88
2. White bread	6.89	1.95	8.30
3. Rice	6.38	2.13	7.85
4. Maize	7.50	2.27	4.6
5. Potatoes	3.07	3.69	3.93
6. Brown bread	13.60	4.26	3.68
7. Peas	6.00	3.57	7.35
8. Carrots	51.33	2.52	3.01
9. Mixed vegetables	.....	3.46	.....
10. Mixed vegetables	.....	4.01	.....

It has been calculated in general that under normal conditions a diet poor in solid residue yields a feces of which the nitrogen amounts to 8 to 9 per cent., with a daily total of 1.14 grammes.

On a diet rich in indigestible constituents, the daily nitrogen amounts to 2.53 grammes, while its percentage falls to 6.6 per cent. As regards the quantity of food, it is a general rule that the more there is eaten, the greater the amount of nitrogen passed out in the feces. On a diet which leaves little residue, the increase is, of course, not so notable. Indeed, up to a certain point, almost all of the constituents of such a diet are digested and absorbed.

Individual variations exist which may considerably modify the amounts excreted on a given diet under normal conditions. Similarly, variations exist owing to exercise, etc.

Pathological conditions may considerably modify both the amount and the percentage of nitrogen excreted in the feces. For example, the quota contributed by the intestine itself may fall considerably in inanition from any cause. On the other hand, it has been suggested that the increase found in such conditions as nephritis, leukemia and gout, is due to a heightened excretion from the body. All conditions which interfere with the proper digestion of the food increase the total nitrogen, although they tend to decrease its percentage, in the manner previously indicated. Gastric diseases have very little influence in this direction, inasmuch as the functions of the stomach are vicariously assumed by the intestines. Biliary obstruction interferes only to a very slight extent with the digestion of the proteids. Failure of the pancreatic secretion, however, may increase the fecal nitrogen enormously, leading to what the French authors describe as azotorrhea.

The other forms of intestinal disease are so complex, that it is, as a rule, impossible to determine whether the increase of nitrogen in the feces be due to deficiency of secretion or absorption, or to increased peristalsis.

Those conditions which are associated with the loss of blood or pus naturally cause an increase in the nitrogen total and percentage. Amyloid and tabes mesaraica increase the nitrogen through failure of absorption.

The most valuable diagnostic hint to be derived from these quantitative examinations has been elucidated by Weintraud. He finds that in pancreatic disease the loss of nitrogenous constituents is far greater than that of fats, a condition which does not maintain in diseases which interfere only with absorption, *e. g.*, amyloid.

Another method has been described for the determination of the proteid residue in the stool, which has not as yet been thoroughly tested, but bids fair to displace that of Kjeldahl. It was

worked out by Koziczkowsky in Senator's clinic, on the basis of a similar method previously used by Meunier and Volhard. Essentially, Koziczkowsky mixes a definite amount of prepared feces with a mixture of HCl and pepsin solution, of which the HCl content is definitely known. This mixture is kept in the incubator for twenty-four hours, after which he determines by titration how much of the free HCl has become bound.

For general diagnostic purposes, it is well to combine the test with the use of a test-diet. Either that previously described, or the following modification, as suggested by Philippsohn, and accepted by Straus, may be used:

First breakfast.—½ liter milk, 2 zwieback.

Second breakfast.—¼ liter bouillon, 1 egg, 1 zwieback.

Noon.—Gruel (¼ liter milk, 1 egg, 20 grammes of oatmeal, and water), 80 grammes scraped beef (boiled with 20 grammes of butter), 200 grammes potato purée.

Afternoon meal.—¼ liter milk, 1 zwieback.

Evening.—Gruel as at noon (without an egg), 2 zwieback, 20 grammes of butter.

The total amounts to: 1½ liters of milk, ¼ liter of bouillon, 6 zwieback, 40 grammes of oatmeal, 40 grammes of butter, 2 eggs, 80 grammes scraped beef, 200 grammes of potato purée. This diet is marked off by carmine or carbon. In making the test, its author used two portions of stool, each equivalent in dry residue to two grammes. These portions were well rubbed up with alcohol, poured into a nitrogen-free filter, washed with absolute alcohol, and then treated in the following fashion: One portion was mixed with 50 cc. of a digestive fluid composed of 1,000 cc. of aqua destillata, HCl (1.19) 10.0, and pepsin 30. The second was mixed with the identical amount of the same mixture after previously rendering it apeptic by cooking three-quarters of an hour in steam. The acidity of both mixtures was then determined, and also their peptonizing strength, by means of Mette's tubes. After twenty-four hours in the incubator, the content of both bottles was filtered, and the amount of free and of combined HCl determined by titration with one-tenth normal soda solution, using dimethylamidoazobenzol and phenolphthalein as indicators.

Considerable labor has been devoted to the differential estimation of the soluble albumins, albumoses and peptones, and of the casein in the stool, but this is of so little practical and diagnostic importance, and is in itself so difficult, that it had best be neglected.

Mucin.—The chemical examination of the feces for mucin is for practical purposes of far less import than the macroscopic or microscopical tests. Of the earlier methods, that of Hoppe-Seyler, which is generally described in the text-books, is unreliable.

In this method, the feces are rubbed up with water, and then an equal quantity of milk of lime is added. After this mixture has stood for several hours, it is filtered, and the filtrate tested with acetic acid. Clouding of the acid is taken as evidence of the presence of mucin. Unfortunately, the method, as has been shown by Gatzky, is far better adapted to reveal the presence of nucleins and nucleo-albumins than of mucin.

The great difficulty with the chemical demonstration of mucin is the fact that mucus secreted in the upper part of the gut is so altered during its passage as to lose its character, while that formed low down in the colon is so dense, and is so permeated by fats and cells, that it is almost insoluble. There is at present, indeed, no satisfactory method for the demonstration of mucin in the feces. Least of all should one expect this with the mucin in solution, as that has almost certainly lost its original properties.

Carbohydrates.—*Sugar.*—The quantitative tests for sugar in the feces, as in urine, are the classical reactions—Trommer's, Nylander's, and the phenyl-hydrazin test. It never occurs normally in adults, and in healthy infants only in minute traces. It is said that dyspeptic and diarrheal conditions in infants are associated with the presence of greater quantities of sugar in the feces.

Starch.—The qualitative determination of starch is most simply made by means of a microscopical examination. In most cases this suffices, but in some it gives a negative result when the macrochemical reaction is positive. The former test consists, as previously described, in adding Gram's solution to the slide preparation under the microscope. In the latter test, the feces are boiled with water, and filtered. The filtrate may be somewhat concentrated by treating over the water-bath, and to it is added a solution of iodine and iodide of potassium in water. The characteristic blue, or bluish-red reaction (erythrodextrin) results.

A variety of quantitative tests have been described, and have been in use, but the best is that described in 1898 by Ad. Schmidt. The patient is placed on test-diet, No. 2, as already detailed. In making the test, it is customary to use five grammes of feces of moderate consistency, using more if the stools are very soft in consistency, and less if hard. The feces are then thoroughly mixed with water and placed in the bottle designated "a" on the figure.

Into tube "b" water is poured. Both "a" and "b" should be quite full, and it is essential for the accuracy of the result that they contain absolutely no air. The apparatus is then adjusted, as shown by Schmidt. Tube "c" has a minute aperture at the tip. The entire apparatus is placed in the incubator at 37° for twenty-four hours, during which time water in "b" is displaced by the gas which is formed in "a." The water displaced is driven into "c," and by its quantity affords a measure of the amount of carbohydrates in the feces. A notion of the actual amount of starch represented by the water displacement is deducible from the fact that the addition of 0.1 gramme of starch to normal feces causes "c," which holds about 30 cc. to be half-filled during the test. Negative results, especially in stools not apparently normal, cannot be taken to indicate the absence of starch, as in abnormal stools the process of fermentation is interfered with. It is important to exclude nitrogenous fermentation, which is done by controlling the reaction with litmus. Carbohydrate fermentation gives an acid reaction, even if slight; nitrogeneous, an alkaline.

The diagnostic value of this test may be considerable, inasmuch as the digestion of starches suffers notably in certain functional and organic diseases of the intestine. Disturbances in the small gut particularly affect the starch digestion. They are generally, but by no means invariably, associated with diarrhea, the so-called "fermentative diarrheas." Gastric conditions do not affect the digestion of starches. Biliary obstruction also, although it results in the production of feces rich in fats, does not interfere with amylolysis. Diseases of the pancreas appear in some cases to exercise a marked inhibitory effect on starch digestion, in others not.

Hydrobilirubin.—There are a number of tests for the presence of hydrobilirubin, of which the best known are the following:

1. *Schmidt's sublimate test.*—Fresh feces are requisite. A piece as large as a hazel or walnut is rubbed up in a mortar with a small amount of concentrated aqueous solution of sublimate, and the mixture is then allowed to stand in a covered watch-glass several hours. The hydrobilirubin is then colored red, the bilirubin green.

Fleischer's test.—A small amount of fecal matter is treated with acid alcohol in a test tube. When the alcohol takes on a brownish color, it is poured off, and a few drops of ammonia are added to it. In the presence of hydrobilirubin the fluid takes on a transparent red color, with greenish fluorescence. The spectroscopic test.—A characteristic absorption band between b and F, nearer F.

Bilirubin.—1. *The sublimate test.*

2. *Gmelin's reaction.*—To nitric acid in a watch-glass is added drop by drop the fecal matter mixed with water, when the characteristic play of colors ensue.

Fat.—The qualitative demonstration of fat in the feces by chemical means is a very simple matter. The feces are extracted with ether, and the latter allowed to evaporate on filter paper, where it deposits a film of fat. The microscopical examination is, however, equally conclusive. The quantitative estimation is of far greater moment, especially the differentiation of the three constituents usually grouped together, viz.: neutral fats, fatty acids and soaps. In certain diseases, this estimation is of very great importance, yet practically the tests are so imperfect and so complicated as to be unavailable for diagnostic purposes. The simplest method is extraction with ether. The test-diet, as previously described, is made use of, and 5 grammes of moderately firm feces (more, if less firm, less if inspissated), are extracted for three days with ether. The extract is then withdrawn, the fat removed by evaporation, and weighed.[1] Another method is the extraction by chloroform (Rosenfeld). Liebermann and Szekely[2] have suggested a saponification method.

Fats, like proteids, are derived both from the body and from the food, and are subject to the same variations as described under that heading, from changes in the quality and quantity of the food, and other causes. Under normal conditions, however, the fats never amount to more than 20 per cent. of the feces, on an average, 7 to 8 grammes a day on a mixed diet. Under pathological conditions, the fats may reach 80 to 90 per cent. of the feces. The conditions which influence fat digestion and absorption are numerous, but those which are really diagnosticible as such from the stools are limited in number. Gastric conditions play a very small rôle, if any, in determining the fat elimination. The existence of a fat-splitting ferment in the stomach, as recently determined, might lead one to expect that achylia would perhaps result in a partial failure of fat digestion. This does not, however, appear to be the case. The most notable changes in fat elimination occur with biliary obstruction. In Fr. Müller's investigations, it was found that with complete biliary obstruction the feces contained 49.1 per cent. of fat instead of about 20 to 25 per cent., as in normal conditions. The effects of pancreatic obstruction on the

[1] Centralblatt f. innere Medicin, 1900, No. 33.

[2] Pflüger's Archiv, 1898, p. 360.

absorption of fats are unfortunately not as yet fully determined, owing to the divergent reports of recent writers on the subject. On the whole, both clinical observation and animal experimentation seem to indicate that pancreatic obstruction causes a notable decrease in fat digestion and absorption. If, however, the fat of the food be in the shape of an emulsion, *e. g.*, in milk, the deficiency is far less marked. Other pathological conditions, such as enteric catarrhs, heart disease, with congestion of the viscera, tabes mesaraica, and amyloidosis may all result in deficiency of fat digestion and absorption, to such an extent that as much as four times the normal amount of fat is thrown out in the feces. A very important factor in the diagnosis of pancreatic obstruction is offered by the relative amounts of neutral fats, on the one hand, and of soaps and fatty acids, on the other, in the stools. Whereas in the feces of adults three-quarters of the fats are split up under normal conditions, in pancreatic disease only one-third to one-fifth are found as soaps and acids, the rest as neutral fats. If, however, the fats of the diet are taken in largely in emulsified form, this difference is very largely lost, inasmuch as the fat-splitting ferment of the stomach is then capable of replacing to a very considerable extent the function of the pancreatic juice.

The diagnostic application of fat determinations in the feces is unfortunately very greatly hampered by the difficulties and complexities of the quantitative methods. The use of a definitely measured test-diet, the quantitative determination of the total residue, and of the total fats, are very laborious procedures. On the other hand, a simple microscopic, or even macroscopic, examination, often suffices to reveal variations of any magnitude from the normal. The diagnostic significance of fat in the stools is summarized as follows by Schmidt and Strasburger: In biliary stasis, the fats are very largely increased in the stools, but fat-splitting is unaffected, and proteid digestion is normal. In disease of the absorptive functions (amyloid, tabes mesaraica) both proteid and fat digestion suffer, the latter, however, in greater degree. Pancreatic disease induces, under certain circumstances, as previously described, very considerable changes in fat digestion, notably in the fermentation of fats, as well as in proteid digestion.

Blood.—Within very recent years, the detection of blood in the feces has become of greater diagnostic importance than had been previously thought to be the case, and concomitant with this discovery there has been some refinement in the methods of the laboratory.

It was first pointed out by Boas that blood in the stools might not only be an indication of intestinal disease, notably new growths, but that it might in many cases afford the only diagnostic evidence of cancer of the stomach. In these cases, however, it is apt to occur in very minute amounts, latent traces, so that much care and refinement of technique is necessary to demonstrate it with certainty.

The older tests for blood are the Teichmann test for hemin, and the turpentine-guaiac test of Schönbein and Almén.

The Teichmann test is performed as follows: A suspected portion of stool is rubbed up with a small quantity of water and acetic acid and then filtered through a piece of cheese-cloth. The filtered material is then precipitated by boiling after alkalinization with sodium hydrate, and the precipitate tested for hemin. A small particle of it is brought on a slide, together with a few crystals of common salt and a drop of glacial acetic acid, and then slowly brought to the steaming point and kept there for about one minute. As the acetic evaporates, fresh acid is added. If hemin be present, the fluid takes on a brownish tinge. It is allowed to cool, and is then examined microscopically. When the test is positive, one finds the so-called hemin crystals, which are hematin chloride. The test is extremely delicate, but very often fails in spite of the presence of blood in the feces. In order to insure its success, both the heating and the cooling should take place very slowly. The reaction also occurs at ordinary room temperatures, if the blood, common salt and acetic be allowed to stand for twenty-four hours, covered by a cover-slip. Of greater practical value, and more commonly used, is the turpentine-guaiac method which has been especially modified to suit the conditions which are found in the feces. It is advisable first to remove the fats from the stool, inasmuch as they interfere with the reaction. This is done by extraction with ether. In case the amount of fat is very considerable, it is wise first to dry out the feces over a water-bath. As a rule, however, the fresh feces may be extracted. Extraction is performed by repeatedly rubbing up a given portion of feces with ether, or by shaking the mixture in a wide-mouthed flask, and renewing the ether several times.

Another difficulty peculiar to the application of this test to the feces or the stomach contents, is the fact, first pointed out by Weber, that the characteristic blue reaction may be induced not only by blood, but by potatoes and other vegetable constituents, also by bile, milk, pus, and other occasional constituents of feces.

It is, therefore, advisable to carry out the test not on the feces, but on an acetic acid extract of them, prepared as follows, according to Weber: A portion of the feces is rubbed up with water, to which one-third of its volume of acetic acid has been added, and the mixture is then extracted with ether. After the mixture has cleared up, a process which may be hastened by the addition of some alcohol, the ether is poured off, and to it are added 10 drops of tincture of guaiac, and 20 to 30 drops of old French oil of turpentine. In the presence of blood, this mixture takes on a bluish-violet tinge. In the absence of blood, it becomes reddish-brown, often with an admixture of grayish-green. The blue coloring matter may be brought out more sharply by adding water and then extracting with chloroform. In making this test, it is very important that the turpentine should be ozonized, as are the old oils. Unless one is sure of its quality, it is best to make a preliminary test of it on a very dilute watery solution of blood. Of late years, considerable doubt has been thrown on the validity of this method for the examination of the feces (Schmilinsky, Koziczkowsky), although it is generally admitted to be a satisfactory test for blood in the stomach contents.

If there is a considerable amount of blood in the stool, the blue reaction is quite marked, and distinct, but in case of small, or minimal quantities, the *terminal reaction* may be marked by a green, brown, or brownish-red, coloration, owing to the obscuration of the primary blue color by the pigment matters of the feces, *e. g.*, urobilin and its derivatives. Such a reaction is, of course, indecisive, and the method is, therefore, at fault in just these cases (carcinoma of the stomach) in which its service would be of supreme importance.

Klunge and Schaer suggested that the test might be made much more delicate by the substitution of a watery solution of Barbadoes aloin for the guaiac, and their contention has been confirmed by an elaborate research carried on in Senator's clinic by Koziczkowsky.[1]

He found that the test reacted to such quantities as 0.025 grammes in 2 grammes of stool. With a test of such extreme delicacy, however, it is necessary to exclude all foods containing blood from the diet, and also to restrict the chlorophyll. A patient in whom there is a suspicion of occult gastric or intestinal hemorrhage, or whose stools have previously given a positive reaction, should be put on a preliminary diet of milk, bread, eggs,

[1] Deutsche med. Wochenschrift, 1904, p. 1198.

fruits and starchy foods. The fats should be restricted, as should also the vegetables, on account of their chlorophyll. This diet is initiated by a dose of carbon (not carmine), which serves to determine the time when the constituents of the previous diet have passed out of the bowel. When the carbon has once made its appearance, the test should be made on the feces on several successive days. A given portion of feces is selected and rubbed up with 10 times its volume of alcohol, in order to remove as much urobilin as possible, inasmuch as its color may obscure the test. The alcohol is then removed by filtration. The fat is then extracted with ether, as previously described. The blood is then to be digested out with glacial acetic, and extracted with ether. It is important to use enough of the former, and not too much of the latter, say 5 grammes of feces, 5 grammes of acid, and 5 to 10 ccm. of ether. If necessary, the acetic acid-ether extract is then filtered clear. This extract is layered over with 1 to 1½ ccm. of ozonized oil of turpentine, and to them are added about 7 to 10 drops of a 3 per cent. solution of aloin. The latter should always be freshly prepared, by dissolving 0.3 grammes of aloin powder in 10 cc. of 60 to 70 per cent. alcohol. The reaction is to be performed in a conical test-tube, *e. g.*, a centrifuge tube.

When the test is performed in this manner, the reaction may occur in one of three ways:

1. The turpentine forms a distinct layer over the etheric extract, and at the junction of the two fluids is seen a very distinct, transparent, reddish ring.

2. The reagents become intimately mixed, and a diffuse reddish coloration results.

3. The turpentine sinks to the bottom, and the red layer is found at the bottom, or tip, of the test-tube. The reddish ring in cases 1 and 3 fades gradually into a reddish discoloration of the neighboring fluid. When the tube is shaken there occurs a diffuse reddish discoloration of the entire liquid. The reaction may occur at once, or only after standing for three to five minutes. If fat has passed over into the etheric extract, it is well to add considerably more turpentine, as it is reduced by the fat.

When the reaction is positive, especially when it has proved so repeatedly, under the prescribed dietetic precautions, it may be positively concluded that there is blood in the feces.

The diagnostic significance of this fact must, of course, be controlled by the clinical findings. Hemorrhages from the nose, mouth, pharynx, stomach, intestines, from polyps, or hemorrhoids,

are, of course, alike capable of giving rise to a positive reaction.

Koziczkowsky, who is authority for the major part of what has been written on this subject, finds that carcinoma of the gastro-intestinal tract in a series of tests give an almost invariably positive reaction. The same cannot be said of ulcers. The presence of blood in the latter is only occasional and intermittent. Its occurrence seems to coincide with the exacerbations of the disease, as denoted clinically by increase of the pain, or vomiting.

The test affords a certain way out of the complexities and difficulties which often beset the physician in the differential diagnosis between organic gastric disease on the one hand, and cholelithiasis, hyperchlorhydria, nervous gastritis, and benign obstruction of the pylorus on the other.

In making the diagnosis on the strength of these findings, it is, however, essential to exclude any cause of hemorrhage below the stomach. The value of the test in cases of intestinal disease is also considerable, especially as clearing up obscure cases of constipation or partial obstruction. Portal or cardiac venous obstruction, with their occasional hemorrhages into the bowel, should, of course, be excluded.

In addition to the chemical tests as previously described, the feces may be spectroscopically examined for the presence of blood, or of any one of the numerous derivatives of blood pigment. Inasmuch as the spectrum is apt to be obscured in the feces, even in the presence of considerable quantities of blood, by the normal pigments in the feces, it is necessary in some way to get rid of these. A further difficulty is the fact that hematin is very imperfectly soluble in water.

To obviate these objections, Sahli recommends the following procedure: A few cubic centimeters of the feces are mixed with water, and sulphuric acid is added drop by drop until the congo reaction is obtained. This mixture is then filtered, and the filtrate extracted with ether. If the ether does not separate properly, a few drops of alcohol may be added. When blood is present, the ether takes on a reddish-brown coloration, and gives the characteristic spectroscopic line of acid hematin in the red. The clinically important spectra are shown in the diagram. Oxyhemoglobin gives two absorption bands, lying between the Traunhofer lines D and E. The band which lies nearest the red end of the spectrum is narrower, darker, and more clearly defined than the other. The former is known as the "a-band," the latter as the "B-band." The

character of the bands is not constant, in all cases, but varies both as to distinctness and breadth, with concentration of the solution of oxyhemoglobin and with the width of the stratum of liquid through which the light passes. If the solution be made extremely dilute, the "B-band" is lost, and the "a-band" becomes extremely faint. With such minimal amounts the chemical examination gives more positive and reliable results. With very strong solutions, the bands fuse. Solutions of reduced hemoglobin show only one band, the "g-band," which also lies between D and E. It is very diffuse, and also varies with the strength of the solution. Methemoglobin is a compound in which the oxygen is held in more stable combination. Its spectrum gives two bands between D and E, and one between C and D. Hematin is obtained through the decomposition of hemoglobin by acids or alkalis in the presence of oxygen. It also has a characteristic spectrum, as shown in the diagram.

CHAPTER XIX.

CHARACTERISTIC PICTURES IN DISEASE.

Acute Enteric Catarrh.—In acute enteritis the diagnosis depends in greater part on an examination of the stools, which also affords the most exact indication of the actual seat of the process.

The feces are of a diarrheal consistency, fluid and frequent. There may be as many as 10 to 15 passages a day, rarely more, the frequency depending largely on the degree of involvement of the large intestine, especially the transverse and descending colon. Indeed, isolated catarrh of the small bowel may run its course without giving rise to diarrhea. At the onset the stools are semi-solid, but rapidly become fluid; even at the height of the disease, however, there may be an occasional well-formed movement.

The stools, when characteristic, are almost watery, and often associated with much foul-smelling gas. The amount of gas and the odor are, however, largely dependent on the nature of the diet and the localization of the catarrhal process. Thus carbohydrates are split up into marsh-gas and certain organic acids, and lend a peculiar odor, and a more acid reaction to the stool. A milk diet gives the odor of butyric acid, and also tends to modify the reaction.

If, however, the catarrh is limited to the colon, these decomposition processes do not go on, and the food is normally digested and absorbed in the small intestine. The character of the stool is then largely determined by the exudates from the wall of the gut.

The color of the dejections varies from a light golden brown to a darker brown than is seen even in normal feces. These variations depend on the degree of oxidation of the biliary pigments, and afford a very valuable indication of the seat of the catarrh. If bilirubin appears in large amounts, giving rise to a yellowish discoloration of the stool, it is always an evidence that the small bowel participates in the affection, and that its contents are hurried through so rapidly that the pigments do not become reduced as normally to urobilin. In children the stools may even be green, from biliverdin, but in adults this is rarely the case. Where biliverdin or bilirubin are present, it is generally possible, in case of the former, always, to obtain the typical Gmelin reaction.

When there is a very profuse serous diarrhea, especially in

colitis, the dejections are often perfectly colorless. This condition is, however, far more frequently found in some of the specific enteric inflammations, *e. g.*, cholera.

Mucus is practically never absent, and affords valuable hints as to the severity and the localization of the process. It may be intimately commingled with the more or less fluid mass, lending to it a jelly-like consistency, or it may merely coat the exterior of the fecal masses in more or less voluminous clumps. The former condition maintains in catarrhs of the small intestine, the latter in colitis. Rarely in acute proctitis, or inflammation of the lower colon, are solid masses of pure mucus expelled. The mucus is often colored with bile pigment, bilirubin or urobilin, which gives further evidence of its origin. It may be clear, hyaline, and transparent, or turbid and opaque. The latter condition is often falsely described as muco-purulent. Microscopical examination, however, reveals the fact that there is an admixture not of pus, but of desquamated epithelia. The latter may be fairly well preserved if derived from the large gut, but if coming from higher portions of the intestine are often entirely disintegrated and fragmented. Pus cells are an extremely rare finding in the stools in cases of pure inflammation. Blood is never found.

The constituents of the diet may appear in more or less unaltered form. This is especially the case when the small intestine is involved, with increase of its peristaltic action, and decrease in its digestive and resorptive capacity. The continued observation of the stools may serve to discover the irritant cause of the catarrh, in the shape of undigested particles of some kind of food, eaten, perhaps, two or three days previous to its passage. The event ordinarily denotes the beginning of a recovery. The chemical examination of the stool in this condition offers little of service. The bacteriological examination is important only in the specific inflammations.

Chronic inflammations of the intestine play a very important rôle in intestinal medicine—a rôle which is none the less important for being rather more limited than is generally supposed. The diagnosis of chronic catarrh is very frequently made in cases of diarrhea or of constipation from a large number of other causes, such as muscular atony, or spasm, or vascular disturbances, or certain organic diseases of the bowel. These latter conditions may all be easily and accurately distinguished from true catarrhs by the character of the stools. Their consistency varies with the degree of activity of the intestinal peristalsis—in cases of diarrhea, thin or semi-fluid; in cases of constipation, even scybalous.

The chief characteristic of importance is the presence of mucus, which, as detailed in the general section, is an almost invariable evidence of catarrhal inflammation. Notable exceptions are the cases of enteritis membranacea, and of the physiological mucoid excretion from the rectum and the colon which accompany many cases of constipation. Mucoid catarrhs are not necessarily primary, but may accompany cancer or ulcer. On the other hand, absence of mucus is almost invariably evidence of the absence of a chronic inflammatory process in the intestine. The amount of mucus varies enormously, as detailed in the general sections. The stool may consist of small portions of mucus commingled with fecal products, or there may be practically nothing except mucus in the dejections. As in acute inflammations, there is neither blood nor pus in the simple catarrhs; but epithelial cells are present in abundance.

The other characteristics of the feces, color, odor, reaction and composition vary in the same degree, and from the same causes, as in cases of acute inflammations. What has been said under that head may be accepted here also.

The frequency of the stool varies greatly in chronic catarrhal processes. Most characteristic are alternating periods of diarrhea and constipation, the periods lasting either days, weeks, or even months. Rarer are continuous constipation or diarrheas.

Purulent Enteritis (Enteritis phlegmonosa vel purulenta).—This very rare condition has not been coprologically studied.

Diphtheritic Enteritis (Enteritis diphtheritica vel crouposa.—There is always diarrhea, often with tenesmus. The stools are fluid, with occasionally the passage of formed feces. They consist chiefly of pus, blood, and mucus. If food is being taken, this is generally mingled in more or less altered condition with the fluid exudate. Sometimes careful search will reveal the presence of macroscopic particles of tissue derived from the wall of the gut. They are, however, generally so altered and necrotic as hardly to be recognizable microscopically. Diphtheritic enteritis, as it occurs in cachetic individuals, *c. g.,* in tuberculosis, carcinoma, etc., is often associated with amyloidosis of the intestinal wall. This results in extremely thin, fluid stools, in which large numbers of pus cells are contained, a condition characterized as blenorrhea intestinalis.

Muco-membranous Colitis (Colica mucosa et enteritis membranacea).—This disease is, as a rule, not associated with frequency of stool. Indeed, the reverse is rather the case. The

dejecta are characteristically composed in greater part, or exclusively, of mucus. This mucus has a tough, leathery consistency, which lends it the capacity to assume and retain certain definite shapes, usually representing a cast of the gut. In this regard, the mucus resembles that produced in certain forms of bronchitis. In shape, it is most frequently tubular, or tape-like, and may present elevations and depressions which are taken to represent casts of the tæniæ and haustra. In color, they are either transparent, or grayish and semi-opaque. They may be stained brown by the admixture of fecal matter, or red (Nothnagel) by blood. The shapes taken by these mucoid masses vary greatly. They occur not only in the typical forms described above, but as clumps, or as dendritiform masses, or as reticula. As a rule, when immersed in water, these various shapes resolve them into the fundamental form of membranes. At first sight, they are mimicked by various other elements which are apt to appear in the feces—fascia, undigested tendon, arteries and veins, orange peelings, curds of milk, or even bacterial conglomerates, such as *Leptothrix*.

Microscopically, the masses are found to consist of mucus, which is typical in its appearance and reactions. In addition, epithelial cells are invariably found, often in enormous amount, frequently well preserved, and again in various degrees of degeneration and alteration. Leucocytes are rare or missing. Eosinophiles, as has previously been stated, are not rarely a concomitant of the condition, in the same manner, possibly, as they are found in cases of bronchial asthma. The chemical analysis of the material voided in this disease reveals in the vast majority of cases that it is composed almost exclusively of mucin. With this are mingled traces of albuminoid substances, globulin or nucleo-albumin, which may, in exceptional cases, even exceed the mucin in amount. Fibrin occurs not at all, or only in traces, the statements of many observers to the contrary notwithstanding.

Ulcers of the Intestine.—The examination of the feces plays a most important part in the diagnosis of ulcers of the intestine. As regards frequency of stool, in cases of ulcer, this may vary enormously. It appears that there may be very numerous and extensive ulcerations of certain parts of the tract without any consequent diarrhea. Thus the small intestine, the cecum, and the ascending colon may be found at autopsy to contain ulcerations, perhaps even very extensive, yet during life there has been normal frequency of defecation or even constipation. A notable example of this condition is presented by many cases of typhoid,

which run their course throughout without diarrhea. Nothnagel says, it is very probable that the diarrheas which do occur in some typhoids must be attributed, as suggested by Cohnheim, in nowise to the ulcerations, but to the irritant action of the typhoid poisons on the gut. Ulcerations of the transverse and descending colon, of the sigmoid loop, and of the rectum especially, almost invariably set up diarrhea, however. Exceptions have been recorded to this rule, as in a case of a phthisica of Kortum's, in whom the descending colon was riddled with tuberculous ulcers, yet there had been only one stool daily. It is possible in such apparent exceptions that the nerve endings in the wall of the gut are destroyed by the ulcerations or paralyzed by the toxins. The stools are, as a rule, rather softer than usual, or even fluid. Here again, the lower the seat of the ulceration, the more characteristic is this symptom. In cases of ileal or jejunal ulcerations, the feces may have quite a normal consistency. If, as in certain cases of chronic ulceration, *e. g.*, in phthisis, amyloidosis is also a factor, the failure of absorption may be due not to the ulcers alone.

The most characteristic symptom of intestinal ulcers is the finding of blood, pus, certain forms of mucus and particles of tissue in the feces. Blood may occur in various ways. If there is a profuse hemorrhage, it is, of course, immediately and easily recognizable, even if the hemorrhage has occurred as high up as the duodenum. On the other hand, there may be only minute hemorrhages, from capillary erosions, and the blood may be so intimately mingled with the fecal matter as to escape detection by macroscopic examination. The higher the seat of the ulcer, the more is the blood altered in its passage, and the more intimately does it become mingled with the fecal masses. In these cases, it is only a microscopical examination or a chemical examination which serves to reveal the blood. Microscopically, one may find either blood corpuscles, more or less altered, or crystals of hematin. The former are more apt to occur in case of colon ulcerations, the latter with disease of the upper bowel. It is very remarkable that the various kinds of ulcers behave very differently with respect to their tendency to bleed. Typhoid and dysenteric ulcers are far more apt to produce hemorrhage than are tuberculous or catarrhal ulcers. Indeed, the latter may run their entire course without any trace of hemorrhage. The significance of blood in the stools is thus formulated by Nothnagel: If blood occurs in the stools under circumstances which permit of the possibility of ulcers, the diagnosis of the latter condition becomes extremely probable. The absence

of blood is no argument against the existence of ulcers. It is important to remember that blood in the stools may occur in case of epistaxis, pharyngeal hemorrhage, and anemias—causes which must be excluded before entertaining the diagnosis of intestinal ulceration.

Pus is even more characteristic than blood in the feces of ulcerative enteritis. Exudation of leucocytes is practically absent in cases of simple catarrh of the intestine, and may be considered pathognomonic of ulceration, whether this be simple or neoplastic. Pus occurs in the feces in certain other rare conditions, *e. g.*, the perforation of extra-intestinal abscesses. The amount of pus varies very greatly. At times, large amounts of almost pure pus are voided. This occurs especially with the perforation of abscesses, with ulcerated carcinomata, and with extensive dysenteric processes. In the majority of cases of simple ulceration, only small amounts of pus pass out in the stool, and very careful search may be necessary to demonstrate them. Characteristic are the minute, yellowish-white clumps, which microscopical examination reveals as conglomerates of pus cells. In many cases, however, the leucocytes are digested and altered beyond recognition in their passage, and this is the more apt to occur, the higher up the seat of the ulceration. Moreover, certain types of ulcer, *e. g.*, the duodenal ulcer, tend not to produce pus. Its absence, therefore, cannot be held to exclude the diagnosis of ulcer. Pure pus is found practically in only two conditions—perforation of extra-intestinal abscesses and diphtheritic enteritis. In dysentery, and in ulcerated carcinomata located in the lower colon and rectum, there is pus mixed in almost equal proportions with blood and mucus.

Shreds of tissue, if of recognizable origin, are direct evidence of ulceration. It is essential to distinguish them from food remnants, a task not always easy. They occur with especial frequency in dysentery, and often in neoplastic ulcerations, while they may be entirely lacking in typhoidal and other ulcerations of the gut. The search for bacteria is often of importance in intestinal ulceration. If a Gram stain is made of the fecal matter, or of a particle of isolated pus, it will generally be found that the stain contains far more Gram positive organisms than is normal, which reveal themselves, on closer examination, as cocci. Not every case of streptococcus enteritis is of necessity ulcerative, but this change in the type of intestinal flora must always be regarded with a high degree of suspicion. The examination for specific organisms is far more difficult, and liable to much error. Tubercle bacilli are a frequent

object of search. Unfortunately, it is practically impossible, by ordinary clinical methods, to differentiate positively between the tubercle bacillus and the hay bacillus, which is often found in normal stools. For this purpose it becomes necessary either to isolate the questionable acid-fast organism by the ordinary method of plate cultures, often a very laborious procedure, and then to test its biological characters, or to determine its pathogenicity by injections into guinea-pigs. But even the presence of demonstrated genuine tubercle bacilli does not prove the existence of an ulcerative tuberculosis of the intestine, inasmuch as the bacilli of the sputum are frequently swallowed in large numbers, and pass out in the feces unaltered. It is only in combination with other positive evidences of ulceration that the presence of tubercle bacilli in the feces should be taken to indicate a specific ulcerative process of the intestine. The finding of dysentery and typhoid bacilli will be treated of more especially in a subsequent subdivision, as will also the presence of amœbæ.

Typhoid. — It was at one time customary to speak of "typhoid stools" as characteristic to a great degree of the disease. They are described as diarrheal, watery, of "pea-soup" like consistency. On standing, they separate into a whitish-yellow, crumbly sediment, and a turbid supernatant fluid. In color they are light yellow; in odor, disagreeable; in reaction, markedly alkaline. It is now well known that this "typical" stool occurs by no means in all cases, and in some epidemics is present in only a small proportion of the cases. Indeed, there may be no diarrhea, and the stools may be normal in form and consistency throughout. The causes underlying the differences are not at all understood. The stools often present slight traces of hemorrhage, which may be evident as red streaks along the exterior of the fecal column, or intimately mingled with it, or may first reveal themselves to microscopic examination. It is believed by Nothnagel that these slight hemorrhages are to be regarded very frequently as the precursors of more profuse losses. Pus cells are present, as is mucus, in small amounts in many cases of typhoid. The examination of the stools for typhoid bacilli has been described in the section on bacteriological technique. The whole matter of typhoid and paratyphoid diagnosis from the stools is constantly becoming more complicated and confused, so that it is difficult at the present moment to decide as to its clinical value. When the Koch school accepted the procedure known as that of Drigalski-Conradi, and previously described, it became customary to identify the doubtful colonies

by means of their agglutinability by high-titer serum of rabbits. In this manner, typhoid bacilli were isolated from the stools in a large proportion of the cases in certain typhoid epidemics, and the paratyphoid form in the same manner in a certain specific epidemic caused by it in the military garrison of Saarbrücken (Conradi). Furthermore, it was not unusual to discover the specific bacilli in the stools of many individuals presenting very slight symptoms, or even none at all, during the time of such epidemics, and these cases were identified by Koch as typhus levissima, or as "immunes," in the same manner as such cases are to be found in every cholera epidemic. Recently it has been found, however, that many true typhoid bacilli do not agglutinate well. Indeed, this fact has been the basis of a subdivision by Sacquepée of the typhoid group into "Eberths," which agglutinate, and "Eberthiformes," which agglutinate poorly. On the other hand, non-typhoid bacilli often agglutinate extremely well with typhoid serum, owing probably to the existence of amboceptors which have more or less affinity for the entire group of related organisms. As a result of these conditions, it might have been expected that very serious confusion would result, as has indeed occurred. Conradi has described cases of paratyphus bacilli in the stools of typhoid patients, Altschüler has found typhoid organisms in the blood of patients whose serum agglutinated paratyphoid in the highest dilution, and Jürgens has obtained such irreconcilable results that he advocates complete disregard of the newer subdivisions, and a return to the old clinical entity of typhoid fever, regardless of cultural determinations. It is, therefore, safe to say that for the present bacteriological examination of the stools should be left to acknowledged experts, and even their results accepted with caution.

Asiatic Cholera and Cholera Nostras.—The stools in Asiatic cholera occasionally resemble those of simple diarrhea, but in the majority of cases they are very characteristic of the condition. In cases of any degree of severity, they no longer resemble feces, but consist of a very thin, fluid material, of a gray or whitish color, in which are suspended minute floccules or granules. These are the characteristic rice-water stools, and they are voided with great frequency, so that during the course of twenty-four hours liters may be lost. The odor of the stools is no longer fecal, but rather albuminous, like spermatic fluid. The reaction is alkaline or neutral. Occasionally the fluid, instead of being colorless, is tinged with red by blood, and then resembles a beef-broth. Chemical examination shows that the fluid contains only 2 per

cent. of solid constituents, of which sodium chloride composes a great part. Of albumin there is little. The finding of cholera bacilli has been already described, and offers an easy method for the identification of the disease.

Dysentery. — The stools in dysentery are characteristically composed of mucus, pus, and blood, mixed in varying proportions in a fluid or semi-solid stool. The stools are not large, but are very frequently voided. Germans distinguish popularly between cases of "white" dysentery, in which the amount of blood lost is small, and "red" dysentery, in which large enough amounts to color the fecal fluid are lost. Peculiarly firm masses of mucus, often partially blood-stained ("carunculæ" of the older authors) are also found. Necrotic masses of mucus membrane are also not rare. The stools may have no odor, or a gangrenous odor. The bacilli are easily found in the mucus.

Amœbic dysentery.—The stools are, as a rule, fluid and frequent. They have a fecal color, and a peculiar, slightly mucilaginous odor. They contain, as a rule, large amounts of mucus, and very often distinct traces of blood. The reaction is invariably alkaline. The microscopic examination of the fresh mucus discloses epithelia, red blood cells, and most characteristic organisms. These having already been described in detail, nothing further need be said of their appearance.

Carcinoma.—The stools of carcinoma of the intestine are characteristic only in case the new growth is situated in the large intestine. Carcinoma of the small gut cannot be diagnosticated from the character of the stools. Several factors, which generally occur in conjunction in cases of new growth of the colon or rectum which have attained any considerable size, combine to alter the character of the stool. These are, the stenosis which it occasions, its ulceration, and the associated catarrh of the bowel. The stenosis occasions a constipation which may persist obstinately for days. In some cases, ulceration of the growth provides a freer passage again, a fact which is generally documented by the initial passage of blood, pus, or fragments of tissue.

Certain cases, on the other hand, present periods of severe diarrhea, due to the catarrh which so frequently accompanies carcinoma. It is very unusual, however, that the diarrheas should persist throughout the course of the disease. As a rule, they are interrupted, or terminated, by a period of constipation due to the obstruction occasioned by the growth. Thus the character of the stools is very variable. At times they are quite normal. Again,

they may show all the earmarks of stenosis; of small caliber, flattened, lead-pencil like, or similar to the stools of goats. Mucus may be present in large amounts, or may be absent, depending on the degree of coincident catarrh. Blood appears in the feces with a considerable degree of frequency, although by no means in all cases. It is most apt to occur in ulcerated new growths, in which case it may appear with regularity in every stool, in larger or smaller amounts, but it is occasionally found in connection with cancers which at autopsy present a perfectly intact surface. In the latter case, it must be supposed that minute hemorrhages are occasioned by the passage of scybalous masses through the narrowed portion of intestine. Pus is found only in case of ulceration, and is generally present in amounts directly commensurate with the loss of surface. In the deeply exulcerated new growths of the colon, pus may be fairly profuse. The presence of any two of these symptoms in the stool, stenotic stools, pus, or blood, points with great probability to the diagnosis of cancer of the colon. Indeed, a mixture of blood and muco-purulent masses, such as is found in many of these cases, occurs in only one other condition, namely, dysenteric ulceration of the intestine, which is, as a rule, easily differentiated by other symptoms. The diagnosis is, of course, definitely determined if one is fortunate enough to discover particles of the new growth itself in the feces, a fairly rare occurrence.

In carcinoma of the rectum, all of the above-mentioned symptoms occur with increased intensity. There is apt to be much blood and pus, and the odor of the stools is often gangrenous.

Amyloidosis.—The diagnosis of intestinal amyloidosis can never be made from the examination of the stools alone, although they afford an essential factor in its recognition. The stools are watery, and contain fecal matter which is generally insufficiently digested. Blood and pus are absent in uncomplicated cases. These characteristics are due to failure of the digestive and of the absorptive faculties of the intestine.

Icterus.—The stools are typically white, alcoholic, and rich in fats. They may be firm, or there may be a diarrhea, set up by the fermentation of the intestinal contents. The fat is usually present as the lime and magnesium salts of the fatty acids, which appear as tufts or sheaves of needle-like crystals. These crystals resist the action of the mineral acids.

Pancreatic Disease.—The essential character of the stools of pancreatic disease depends upon the fact that with it the

intestine is robbed of its digestive ferments. As is well known, all three of the chief constituents of the diet—starches, proteids and fats—depend at once on the pancreatic juice for their complete alteration, and in its absence the process of digestion is almost completely inhibited. To a certain extent, the starches and fats, altered and split up by the gastric juice and by the bacteria, are still capable of absorption, but in most cases a great portion of them passes out in the feces partially undigested. The proteid constituents, muscle fibers, etc., are most apt to be found in the stools, characteristically in fairly large masses. Fats are found typically as globules of neutral fat, but may be entirely absent from the stool. Starches are an evidence of the most severe disturbances. They occur in pancreatic disease, as a rule, only when conjoined with a very active peristalsis which hurries the food with more than normal rapidity through the gut. Otherwise there are no characteristic alterations of the stool in pancreatic disease.

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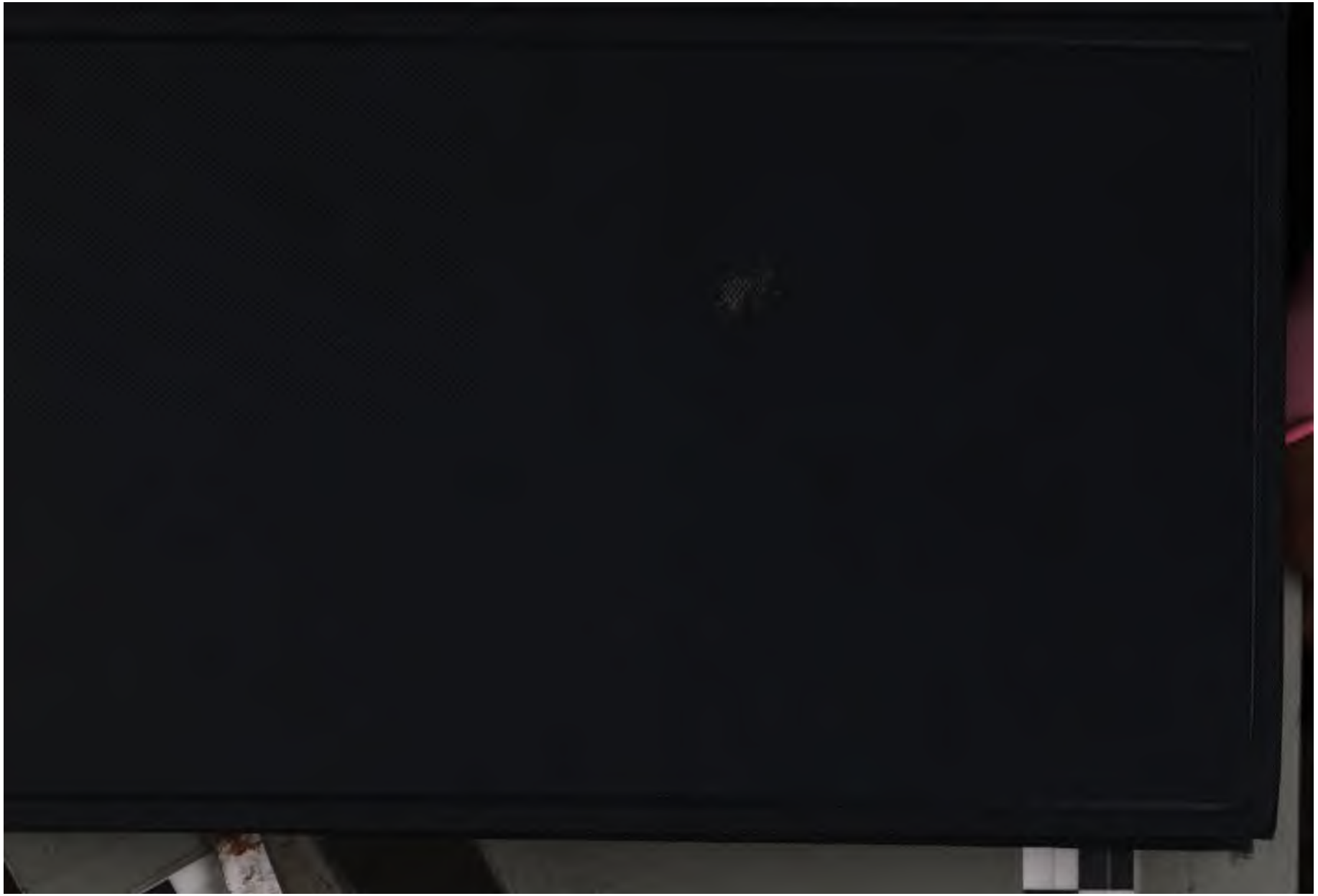
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